ICAFVP

1. ULUSLARARASI TARIM, GIDA, VETERİNER VE ECZACILIK BİLİMLERİ KONGRESİ

18 - 21 Ocak 2023

Kazablanka

ACADEMY GLOBAL CONFERENCES & JOURNALS

www.akademikongre.org

ICAFVP

1ST INTERNATIONAL CONFERENCE ON AGRICULTURE, FOOD, VETERINARY AND PHARMACY SCIENCES

January 18 - 21, 2023

Casablanca

CREATIVE • INNOVATION • TEAM WORK

www.icafvp.com

AKADEMİ KONGRE- DERGİ- EĞİTİM- YAYINCILIK

ISBN: 978-625-6393-12-7

Academy Global Publidhing House

ICAFVP
1ST INTERNATIONAL CONFERENCE ON AGRICULTURE, FOOD, VETERINARY AND PHARMACY SCIENCES
JANUARY 18 - 21, 2023
CASABLANCA

Edited By
PROF. DR. ALİ BİLGİLİ

CONGRESS ORGANIZING BOARD
Head of Conferece: *Prof. Dr. Ali BİLGİLİ*
Head of Organizing Board: *Assit. Prof. Dr. Gültekin Gürçay*
Organizing Committee Member: *Prof. Dr. Naile BİLGİLİ*
Organizing Committee Member:: *Prof. Dr. Başak HANEDAN*
Organizing Committee Member:: *Prof. Dr. Raihan YUSOPH*
Organizing Committee Member: *Prof. Dr. Hajar HUSEYNOVA*
Organizing Committee Member: *Assoc. Prof. Dr. Könül Səmədova*
Organizing Committee Member: *Aynurə Əliyeva*
Organizing Committee Member: *Doç. Dr. Nazilə Abdullazadə*
Organizing Committee Member: *Doç. Dr. Sevinc Sadıqova*
Organizing Committee Member: *Dr. Mehdi Meskini Heydarlou*
Organizing Committee Member: *Doç. Dr. Könül Səmədova*
Organizing Committee Member: *Dr. Amaneh Manafidizaji*

All rights of this book belong to Academöy Global Publishing House
Without permission can't be duplicate or copied.
Authors of chapters are responsibleboth ethically and juridically.
Academy Global–2023©

Issued: 15.02.2023
ISBN: 978-625-6393-12-7

CONFERENCE ID

ICAFVP
1ST INTERNATIONAL CONFERENCE ON
AGRICULTURE, FOOD, VETERINARY AND PHARMACY SCIENCES

DATE – PLACE
JANUARY 18 - 21, 2023
CASABLANCA

ORGANIIZATION
ACADEMY GLOBAL CONFERENCES & PUBLISHING

EVALUATION PROCESS
All applications have undergone a double-blind peer review process.

PARTICIPATING COUNTRIES
Turkey – Malaysia - Iran - India- Croatia – Latvia – Uzbekistan – Morocco – Belgium- France – Algeria – Iraq – Indonesia – Saudi Arabia

PRESENTATION
Oral presentation

PERCENTAGE OF PARTICIPATION
45% FROM Turkey And 55% From Other Counteries

LANGUAGES
Turkish, English, Russian, Persian, Arabic

Scientific & Review Committee

Dr. Gulmira ABDİRASULOVA – Kazakhstan

Prof. Dr. Yunir ABDRAHIMOV – Russia

Doç. Dr. Nazilə Abdullazadə - Azerbaijan

Dr. Omid AFGHAN - Afghanistan

Prof. Dr. Burcu Semin AKEL - Türkiye

Dr. Maha Hamdan ALANAZİ - Saudi Arabia

Aynurə Əliyeva - Azerbaijan

Dr. Dzhakipbek Altaevich ALTAYEV - Kazakhstan

Doç. Dr. Abdulsemet AYDIN – Türkiye

Doç. Dr. Mehmet Fırat BARAN - Türkiye

Dr. Amina Salihi BAYERO – Nigeria

Prof. Dr. Ali BILGILI – Türkiye

Prof. Dr. Naile BİLGİLİ - Türkiye

Prof. Dr. Başak HANEDAN - Türkiye

Dr. Baurcan BOTAKARAEV - Kazakhstan

Dr. Ahmad Sharif FAKHEER - Jordania

Doç. Dr. Abbas GHAFFARI – Iran

Dr. Gültekin GÜRÇAY – Türkiye

Prof. Dr. Gulzar İBRAGİMOVA - Azerbaijan

Doç. Dr. Dilorom HAMROEVA - Ozbekstan

Dr. Dody HARTANTO - Indonesia

Dr. Mehdi Meskini HEYDALOU – Iran

Prof. Dr. Həcər Hüseynova - Azerbaijan

Dr. Bazarhan İMANGALİYEVA - Kazakhstan

Dr. Keles Nurmaşulı JAYLIBAY - Kazakhstan

Dr. Mamatkuli JURAYEV – Ozbekistan

Dr. Kalemkas KALIBAEVA – Kazakhstan

Dr. Bouaraour KAMEL – Algeria

Prof. Dr. Hülya Çiçek KANBUR - Türkiye

Doç. Dr., İradə Kərimova - Azerbaijan

Prof. Dr. Emine KOCA – Türkiye

Prof. Dr. Fatma KOÇ - Türkiye

Prof Dr. Bülent KURTİŞOĞLU - Türkiye

Prof. Dr. Natalia LATYGINA - Ukraina

Sonali MALHOTRA - India

Dr. Alia R. MASALİMOVA - Kazakhstan

Prof. Muntazir MEHDI - Pakistan

Dr. Amanbay MOLDIBAEV - Kazakhstan

Assist. Prof. K. R. PADMA – India

Doç. Dr. Sevinc Sadıqova - Azerbaijan

Doç. Dr. Yeliz ÇAKIR SAHİLLİ - Türkiye

Dr. Ayslu B. SARSEKENOVA - Kazakhstan

Doç. Dr. Könül Səmədova - Azerbaijan

DR. Bhumika SHARMA - India

Dr. Gulşat ŞUGAYEVA – Kazakhstan

Prof. Dr. Dwi SULISWORO – Indonesia

Assoc. prof. Ivaylo STAYKOV, Bulgaria

Dr. K.A. TLEUBERGENOVA - Kazakhstan

Dr. Cholpon TOKTOSUNOVA – Kirgizia

Dr. Hoang Anh TUAN - Vietnam

Dr. Botagul TURGUNBAEVA - Kazakhstan

Dr. Dinarakhan TURSUNALİEVA - Kirgizia

Prof. Dr. Raihan YUSOPH -Philippines

Prof.Dr. Akbar VALADBIGI - Iran

Dr. Yang ZİTONG - China

ICAFVP 1st International Conference On Agriculture, Food, Veterinary And Pharmacy Sciences
January 18 - 21, 2023
Casablanca

Conference Organizing Committee

Chair: Prof. Dr. Ali Bilgili
Organizing Committee Member: Assist. Prof. Dr. Gültekin Gürçay
Organizing Committee Member: Prof. Dr. Naile Bilgili
Organizing Committee Member: Prof. Dr. Başak Hanedan
Organizing Committee Member: Prof. Dr. Hülya Çiçek Kanbur
Organizing Committee Member: Prof. Dr. Raihan Yusoph
Organizing Committee Member: Assoc. Prof. Dr. K. R. Padma
Organizing Committee Member: Prof. Dr. Həcər Hüseynova
Organizing Committee Member: Assoc. Prof. Dr. İradə Kərimova
Organizing Committee Member: Assoc. Prof. Dr. Könül Səmədova
Organizing Committee Member: Assoc. Prof. Dr. Nazilə Abdullazadə
Organizing Committee Member: Assoc. Prof. Dr. Sevinc Sadıqova
Organizing Committee Member: Assist. Prof. Dr. Zemfira Abbasova
Organizing Committee Member: Amaneh Manafidizaji
Organizing Committee Member: Aynurə Əliyeva
Organizing Committee Member: Assist. Prof. Dr. Mehdi Meskini Heydalou

Join Zoom Meeting
https://us02web.zoom.us/j/88193707664?pwd=WGVicnM0d204dmViVEU5Z00xSUR0UT09

Meeting ID: 881 9370 7664
Passcode: 210123

IMPORTANT, PLEASE READ CAREFULLY

- To be able to make a meeting online, login via https://zoom.us/join site, enter ID instead of "Meeting ID
- or Personal Link Name" and solidify the session.
- The Zoom application is free and no need to create an account.
- The Zoom application can be used without registration.
- The application works on tablets, phones and PCs.
- Speakers must be connected to the session **10 minutes before** the presentation time.
- All congress participants can connect live and listen to all sessions.
- During the session, your camera should be turned on **at least %70** of session period
- Moderator is responsible for the presentation and scientific discussion (question-answer) section of the session.

TECHNICAL INFORMATION

- Make sure your computer has a microphone and is working.
- You should be able to use screen sharing feature in Zoom.
- Attendance certificates will be sent to you as pdf at the end of the congress.
- Moderator is responsible for the presentation and scientific discussion (question-answer) section of the session.
- Before you login to Zoom please indicate your name surname and hall number,

exp. H-..., S- ... NAME SURNAME

21.01. 2023	11: 00 – 13:00 Time zone in Turkey (GMT+3)
Meeting ID: 881 9370 7664	**Passcode: 210123**

HALL: 1 SESSION: 1	MODERATOR: **Assist. Prof. Merve YURTTAŞ**
Siham Bouahim **Laila Rhazi** **Btissam Amami** **Aline Waterkeyn** **Mouhssine Rhazi ,** **Er-Riyahi Saber** **Abdelmjid Zouahri** **Maarten Van den Broeck** **Serge D.Muller** **Luc Brendondk** Patric Grillas	UNRAVELING THE IMPACT OF ANTHROPOGENIC PRESSURE ON PLANT COMMUNITIES IN MEDITERRANEAN TEMPORARY PONDS
Assist. Prof. Merve YURTTAŞ	DETERMINATION OF IN VITRO ANTIMICROBIAL ACTIVITY AND ESSENTIAL OIL COMPONENTS OF THYME PLANT
Doç. Dr. Emine NAKİLCİOĞLU **Selen SEYHAN** Eda NURKO	ÇAY YAPRAKLARINDAKİ DEĞERLİ AMİNO ASİT: TEANİN
Prof. A. Anorbaev A. Raxmanov	EFFECTIVENESS OF NEW CHEMICALS IN THE MANAGEMENT OF THE AMOUNT OF APPLE RED MITE (PANONYCHUS ULMI KOCH)
NİHAL BALTACI SEMİHA ERİŞEN	GÜMÜŞ NİTRAT VE GÜMÜŞ NANOPARTİKÜLLERİN SALVİA OFFİCİNALİS BİTKİSİNDE ROSMARİNİK ASİT VE KAFEİK ASİT İÇERİĞİNE ETKİSİ
ABOUREJAL Nesrine **BENAMARA Salim** **HADJ MIMOUNE Khadidja** GHORZI Ikram	ASSESSMENT OF METAL LEVELS IN TEA
Asst. prof., FADİME CANBOLAT	EVALUATION OF PHARMACOKINETIC PROPERTIES OF PIPER METHYSTICUM AND VALERINA OFFICINALIS PLANT INGREDIENTS WITH SEDAATIVE EFFECTS BY IN SILICO ANALYSIS METHOD
Ghulam Murtaza, Kalsoom Farzana	SALBUTAMOL SULPHATE-ETHYLCELLULOSE TABLETTED MICROCAPSULES: PHARMACOKINETIC STUDY USING CONVOLUTION APPROACH

21.01. 2023	11: 00 – 13:00 Time zone in Turkey (GMT+3)
Meeting ID: 881 9370 7664	**Passcode: 210123**

HALL: 2 SESSION: 1	MODERATOR: **Prof. Dr. BAŞAK HANEDAN**
Chenyang Liu Cuixia Li	EVALUATION OF CARBON EMISSION EFFICIENCY AND THE INFLUENCING FACTORS OF DAIRY FARMS IN CHINA UNDER THE CARBON PEAKING AND CARBON NEUTRALITY GOAL
Doç. Dr. Emine NAKİLCİOĞLU Dr. Ceyda DADALI Gizem TİRYAKİ	YUMURTA KABUĞU ATIĞININ DEĞERLENDİRİLMESİ
Dr. Öğr. Üyesi Tarık ŞAFAK	INVESTIGATION OF BLOOD GAS PARAMETERS IN SHEEP WITH TORSION UTERI
Dr. Öğr. Üyesi Şükrü DEĞİRMENÇAY Arş. Gör. Emre EREN Dr. Öğr. Üyesi Sıtkıcan OKUR	ANALYSIS FINDINGS OF CEREBROSPINAL FLUID IN A DOG WITH NERVOUS DISTEMPER
Prof. Dr. ALİ BİLGİLİ Prof. Dr. BAŞAK HANEDAN	EHRLICHIOSIS IN DOGS AND DIFFERENT THERAPY CHOICES
Prof. Dr. ALİ BİLGİLİ Prof. Dr. BAŞAK HANEDAN	PERITONITIS IN CATS AND DIFFERENT THERAPY CHOICES
CANSU AYDIN BÜŞRA ALAN ZEKİ SERİN Dr. Öğr. Üyesi, SELİN ÖZKAN KOTİLOĞLU Prof. Dr., SERAP YALÇIN AZARKAN	INVESTIGATION OF THE PROLIFERATIVE AND METASTATIC EFFECTS OF PYRACLOSTROBIN ON HUMAN MCF-7 AND MDA-MB-231 BREAST CANCER CELL LINES
CANSU AYDIN BÜŞRA ŞENTÜRK Dr. Öğr. Üyesi, SELİN ÖZKAN KOTİLOĞLU Prof. Dr., SERAP YALÇIN AZARKAN	CYTOTOXIC EFFECTS OF FLUORENE-9-BISOHENOL (BPFL) ON HUMAN MCF-7 AND MDA-MB-231 BREAST CANCER CELL LINES

21.01. 2023 **Meeting ID: 881 9370 7664**	11: 00 – 13:00 Time zone in Turkey (GMT+3) **Passcode: 210123**
HALL: 3 SESSION: 1	MODERATOR: **DR. MARYAM AZIZKHANI**
Behrouz Mosayebi Dehkordi	OPTIMIZATION THE PROCESS OF OSMO – CONVECTIVE DRYING OF EDIBLE BUTTON MUSHROOMS USING RESPONSE SURFACE METHODOLOGY (RSM)
Zainoldin, K.H. Baba, A.S.	THE EFFECT OF HYLOCEREUS POLYRHIZUS AND HYLOCEREUS UNDATUS ON PHYSICOCHEMICAL, PROTEOLYSIS, AND ANTIOXIDANT ACTIVITY IN YOGURT
PHD Candidate Bharti Negi Dr. Gargi Dey	COMPARATIVE ANALYSIS OF TOTAL PHENOLIC CONTENT IN SEA BUCKTHORN WINE AND OTHER SELECTED FRUIT WINES
Maja Benkovic, Ingrid Bauman	FLOW PROPERTIES OF COMMERCIAL INFANT FORMULA POWDERS
Dr. Maryam Azizkhani, Parvin Zandi	EFFECTS OF SOME NATURAL ANTIOXIDANTS MIXTURES ON MARGARINE STABILITY
Marzieh Moosavi-Nasab, Mohsen Gavahian, Ali R. Yousefi, Hamed Askari	FERMENTATIVE PRODUCTION OF DEXTRAN USING FOOD INDUSTRY WASTES
Assist. Prof. Dr. Vita Levkane, Sandra Muizniece-Brasava, Dr. Lija Dukalska	SOUS VIDE PACKAGING TECHNOLOGY APPLICATION FOR SALAD WITH MEAT IN MAYONNAISE SHELF LIFE EXTENSION
Ibrahim Mohammed Saeed Shnawa	TUBERCULIN, TETANUS IMMUNOGLOBULIN AND DPT VACCINE AS AN AVIAN IN VIVO T- LYMPHOCYTE MITOGENS
Diah Tri Widayati	EMBRYO TRANSFER AS AN ASSISTED REPRODUCTIVE TECHNOLOGY IN FARM ANIMALS
Raniah Al-Shalabi, Omaima Al- Gohary, Samar Afify, Eram Eltahir	COMPARATIVE EVALUATION OF THE BIOPHARMACEUTICAL AND CHEMICAL EQUIVALENCE OF THE SOME COMMERCIAL BRANDS OF PARACETAMOL TABLETS

Content

Confeence ID

Scientific & Review Committee

Program

Content

Oral Presented Papers In The Confernce

Unraveling The Impact Of Anthropogenic Pressure On Plant Communities In Mediterranean Temporary Ponds 1
Siham Bouahim, Laila Rhazi, Btissam Amami, Aline Waterkeyn, Mouhssine Rhazi , Er-Riyahi Saber, Abdelmjid Zouahri , Maarten Van den Broeck, Serge D. Muller, Luc Brendondk &Patric Grillas

DETERMINATION OF IN VITRO ANTIMICROBIAL ACTIVITY AND ESSENTIAL OIL COMPONENTS OF THYME PLANT 2
Merve YURTTAŞ

ÇAY YAPRAKLARINDAKİ DEĞERLİ AMİNOASİT: TEANİN 8
Emine NAKİLCİOĞLU, Selen SEYHAN , Eda NURKO

Effectiveness Of New Chemicals In The Management Of The Amount Of Apple Red Mite (Panonychus Ulmi Koch) 15
A Anorbaev, A Raxmanov

Gümüş Nitrat ve Gümüş Nanopartiküllerin Salvia officinalis Bitkisinde Rosmarinik Asit ve Kafeik Asit İçeriğine Etkisi 22
NİHAL BALTACI , SEMİHA ERİŞEN

YUMURTA KABUĞU ATIĞININ DEĞERLENDİRİLMESİ 23
Emine NAKİLCİOĞLU, Ceyda DADALI, Gizem TİRYAKİ

INVESTIGATION OF BLOOD GAS PARAMETERS IN SHEEP WITH TORSION UTERI 27
Tarık ŞAFAK

NERVÖZ DİSTEMPERLİ BİR KÖPEKTE BEYİN OMURİLİK SIVISI ANALİZ BULGULARI 28
Şükrü DEĞİRMENÇAY, Emre EREN, Sıtkıcan OKUR

KÖPEKLERDE ERLİŞİYOZİS VE FARKLI SAĞALTIM SEÇENEKLERİ 30
ALİ BİLGİLİ, BAŞAK HANEDAN

KEDİLERDE PERİTONİTİS VE FARKLI SAĞALTIM SEÇENEKLERİ 33
ALİ BİLGİLİ, BAŞAK HANEDAN

PİRAKLOSTROBİN'İN İNSAN MCF-7 ve MDA-MB-231 MEME KANSERİ HÜCRE HATLARI ÜZERİNDEKİ PROLİFERATİF VE METASTATİK ETKİLERİNİN ARAŞTIRILMASI 36
CANSU AYDIN, BÜŞRA ALAN , ZEKİ SERİN , SELİN ÖZKAN KOTİLOĞLU , SERAP YALÇIN AZARKAN

FLUORENE-9-BİSFENOL (BPFL)' ÜN İNSAN MCF-7 VE MDA-MB-231 MEME KANSERİ HÜCRE HATLARI ÜZERİNDEKİ SİTOTOKSİK ETKİLERİ 38
CANSU AYDIN, BÜŞRA ŞENTÜRK, SELİN ÖZKAN KOTİLOĞLU, SERAP YALÇIN AZARKAN

EVALUATION OF PHARMACOKINETIC PROPERTIES OF *PIPER METHYSTICUM* AND *VALERINA OFFICINALIS* PLANT INGREDIENTS WITH SEDATIVE EFFECTS BY IN SILICO ANALYSIS METHOD 40
FADİME CANBOLAT

Optimization of the Process of Osmo – Convective Drying of Edible Button Mushrooms Using Response Surface Methodology (RSM) 55
Behrouz Mosayebi Dehkordi

The Effect of Hylocereus polyrhizus and Hylocereus undatus on Physicochemical, Proteolysis, and Antioxidant Activity in Yogurt 56
Zainoldin, K.H., Baba, A.S.

Comparative Analysis of Total Phenolic Content in Sea Buckthorn Wine and Other Selected Fruit Wines 57
Bharti Negi, Gargi Dey

Flow Properties of Commercial Infant Formula Powders 58
Maja Benkovic, Ingrid Bauman

Effects of Some Natural Antioxidants Mixtures on Margarine Stability 59
Maryam Azizkhani, Parvin Zandi

Fermentative Production of Dextran using Food Industry Wastes 60
Marzieh Moosavi-Nasab, Mohsen Gavahian, Ali R. Yousefi, Hamed Askari

Sous Vide Packaging Technology Application for Salad with Meat in Mayonnaise Shelf Life Extension 61
Vita Levkane, Sandra Muizniece-Brasava, Lija Dukalska

Tuberculin, Tetanus Immunoglobulin and DPT Vaccine as an Avian in vivo T- Lymphocyte Mitogens 62
Ibrahim Mohammed Saeed Shnawa

Embryo Transfer as an Assisted Reproductive Technology in Farm Animals 63
Diah Tri Widayati

Comparative Evaluation Of The Biopharmaceutical And Chemical Equivalence Of The Some Commercial Brands Of Paracetamol Tablets 64
Raniah Al-Shalabi, Omaima Al- Gohary, Samar Afify, Eram Eltahir

Salbutamol Sulphate-Ethylcellulose Tabletted Microcapsules: Pharmacokinetic Study using Convolution Approach 65
Ghulam Murtaza, Kalsoom Farzana

Unraveling The Impact Of Anthropogenic Pressure On Plant Communities In Mediterranean Temporary Ponds

Siham Bouahim[1,3,7], Laila Rhazi[1], Btissam Amami[1,3,7], Aline Waterkeyn[2,3 4] , Mouhssine Rhazi [4], Er-Riyahi Saber[5], Abdelmjid Zouahri [6] , Maarten Van den Broeck[2,1], Serge D. Muller[7], Luc Brendondk [2]&Patric Grillas[3]

1. Hassan II Casablanca University, Faculty of Sciences Aïn Chock, Laboratory of Aquatic Ecology and Environment, BP 5366, Maarif, Casablanca, Morocco 2

2 . Laboratory of Aquatic Ecology, Evolution and Conservation , Katholieke Universiteit Leuven, 32, 3000, Belgium

3. Tour du Valat, Research Centre for Mediterranean Wetlands, Le Sambuc, 13200 Arles, France

4. Moulay Ismail University, Faculty of Sciences and Techniques, Department of Biology, BP 509, Boutalamine, Errachidia, Morocco

5. Moulay Ismail University, Faculty of Letters and Human Sciences, Department of Geography, BP 11202, Zitoune Meknès, Morocco

6. Agronomic National Research Institute (INRA), CRRA of Rabat, BP 415 RP, Rabat, Morocco

7. Université Montpellier2 - CNRS, Institut des Sciences de l'Evolution, Case 061, 34095 Montpellier cedex 05, France

Abstract

Identifying the respective role of environmental, landscape and management factors in explaining the patterns in community composition is an important goal in ecology.

Using a set of 32 temporary ponds in Northern Morocco we studied the respective importance of local (within the pond), regional (density of ponds in landscape) factors and the impacts of land uses on the plant species assemblages separating Pond and Opportunistic species. The main hypotheses tested were that (1) species assemblages respond to both local and regional environmental factors, (2) anthropogenic pressure has a negative influence on the number of Pond species, and that (3) human activities differ in their impact on pond biodiversity. The results showed that (1) local factors explain most of the variation in the species composition of plant communities, (2) land use impacts the communities through changing local environmental conditions, leading to a loss of characteristic Pond species. Except recreation, all other activities (grazing, drainage, agriculture and partial urbanization) significantly reduced Pond species diversity. The conservation strategy for rare Mediterranean temporary Pond species should focus on networks of oligotrophic ponds which contain the species with highest conservation value and consider only those uses which are compatible with sustainable management of the ponds.

DETERMINATION OF IN VITRO ANTIMICROBIAL ACTIVITY AND ESSENTIAL OIL COMPONENTS OF THYME PLANT

Merve YURTTAŞ

Amasya University, Faculty of Health Science, Department of Nutrition and Dietetics, Amasya/Turkey

Abstract

Thyme is an aromatic plant in the Lamiaceae family. Thymol and carvacrol, which are intensely present essential oils in thyme, give a pleasent smell to thyme and also provide antimicrobial activity. Studies on herbal additives have increased due to the fact that food consumers do not want to use synthetic additives due to serious side effects and demand for natural ones. In this study essential fatty acids of dried thyme plant obtained from a herbalist (Çorum province/Turkey) were determined and its antimicrobial activity is investigated against some bacteria by disk difusion method. As a result, thymol was found to be the most concentrated component (%26.30) among thyme essential fatty acids, thyme showed that the highest antimicrobial activity against *S.aureus* bacteria (56 mm) among the tested microorganisms.

Keywords: thyme, essential oil, antimicrobial activity

1. INTRODUCTION

Medicanal and aromatic plants have been a part of our lives all over the world since ancient times. These plants are known to be used as preservatives in pharmaceuticals, cosmetics and foods (Varlı et al, 2020). The use of plants in treatment of diseases dates back to prehistoric times. It has been stated that the plant used in the treatment of diseases in medicanal applications is called “medical plants” (Özderin et al, 2014). In the literatüre it is stated that medicanal and aromatic plants have many properties such as antimicrobial, antifungal, anticancer, antihistamine, antiinflammatory, antiokxidant, pain reliever (Bayaz, 2014; Sakkas and Papadopoulou, 2017; Varlı et al, 2020). These properties of plants are due to the fact that they have active substances such as steroids, flavonoids, saponins, alkaloids, terpenes, and phenolic compounds (Kürekci and Sakin, 2017). Their activities on diseases vary depending on the type and amount of these active substances (İlkimen and Gülbandılar, 2018; Tural and Turhan, 2017). In recent years the use of natural ingredients has increased in many commercial areas (pharmaceuticals, cosmetics, food, etc.) due to the potential dangers of synthetic additives (Bayaz, 2014). Thyme is just one of thousands of medicanal and aromatic plants. Thyme is an aromatic plant in the Lamiaceae family, which has a distinctive smell, loves heat and can grow many areas (Ertürk et al, 2010). It is stated in various sources that thyme has digestive stimulant, antimicrobial, antioxidant, antispasmadic properties (Rota et al, 2008; Ertürk et al, 2010; Faydaoğlu and Sürücüoğlu, 2013; Kürekci ve Sakin, 2017). Thymol and carvacrol subtances are concentrated in thyme and these active substances are known to have antimicrobial properties. (Baydar, 2005; Benli and Yiğit, 2005). In this study it was aimed to determine the essential oil components of thyme plant and its antimicrobial activity against some bacteria.

2. MATERIAL METHOD

2.1 Extraction of essential oils

The research material was obtained in dried form from a herbalist (Çorum province/Turkey) which spices are widely sold. 100 g of plant sample were distilled for 3 hours by in a

hydrodistillation device with Clevenger apparatus (El Hattabi et al, 2016). The obtained thyme essential oil was used in antimicrobial activity test and ıt was stored in a deep freezer at -20°C to detect essential components. Analysis were repeated 3 times.

2.2 Antimicrobial activity test

Antimicrobial activity of thyme extract was determined by disc diffusion method (CLSI, 2011). Therefore *Staphylococcus aureus* ATCC 25923, *Streptococcus mutans* ATCC 9027, *Bacillus subtilis* ATCC 6633, *Salmonella enteritidis* ATCC 13076, *Pseudomonas aeruginosa* ATCC 9027, *Klebsiella pneumania* ATCC 70603 bacterial strains have been used. Microorganisms were seeded on Triptic Soy Agar and incubated for 24 hours at 37°C and activated. Mueller Hinton Agar (MHA) has been used for antimicrobial activity. Bacterias from 24h culture were adjusted to 0.5 MacFarland using saline. This liquid culture was inoculated into MHA medium with a sterile swab. After planting, sterile disc with 20 μl thyme oil was impregnated on MHA medium and gentamicin and chloramphenicol antibiotics discs were left 20 mm apart from each other and outside petri dish to measure antibiotic sensitivity. Petri dishes were incubated for 24-48 hours at 37°C and inhibition zone diameter around the disc was measured with a caliper.

2.3 Detection of essential oils components

Determintion of essential oil components of thyme was carried out with the service of (Agilent brand GC-MSD-7890B GC-5977MSD) Amasya University Central Research and Application Laboratory. CB WAX, 60 mm x 250 µm x 0.25 µm long column and Helium (1 ml/min flow rate) gas as carrier gas wae used in device. Temperature program reaches from 40°C to 240°C in 4°C/min increments. Injection block is 240°C ve detector temperature is 250°C. (Nejad Ebrahimi et al, 2008; Koçer 2021).

3. RESULT AND DISCUSSION

Antimicrobial activity zone diameters of thyme against some bacteria are given in Table 1.

Table 1. Antimicrobial activity results of thyme extract

	Gentamicin(CN)	Chloramphenicol (C)	Thyme
S. aureus	24	26	56
S. mutans	23	26	54
B. subtilis	29	27	16
S. enteritidis	15	20	18
P. aureginosa	16	27	24
K. pneumania	17	22	29

As seen in Table 1 zone diameters of thyme oil against test microorganisms ranged between 16-56 mm and it was determined that it showed antimicrobial activity against all bacteria. In this study, it was determined that thyme oil showed high antimicrobial activity against *S.aureus* (56 mm) and *Streptococcus mutans* (54 mm) bacteria. Thyme showed moderate activity against *S.enteritidis* and *B.subtilis* bacteria with an inhibition diameter of 18 and 16 mm. In the studies by Tural and Turhan (2017), Kılıç (2019) and Uçar et al (2015) the zone diameter of thyme against *S.aureus* bacteria was 39.33; 49.27 and 40 mm respectively. In the study conducted by Fani and Kohanteb (2017) at various concentrations, antimicrobial activity zone diameter of thyme against *S.mutans* bacteria was measured 38 mm. Thyme essential oil by Borugă et al (2014) study has high antimicrobial activity against *S. aureus* and *K.pneumania* bacteria. In

anaother study by Nalbantbaşı and Gölcü (2009), it was determined that thyme showed antimicrobial activity (7 mm) on *Bacillus subtilis*.

Essential oil components ot the thyme plant are given in Table 2. In this study when essential oil components were examined, the highest component was determined as thymol (%26.30). The highest component was determined as thymol by Özderin et al (2014). In the study conducted by Borugă et al (2014), main component of thyme plant (*Thymus vulgaris*) grown in Romania was found to be thymol (%47.59). the main component of thyme was determined as thymol with ratio of %30.20 and %48.1, respectively. In the study conducted by El Hattabi et al, (2016), carvacrol component was found to be the most concentrated component with %78.4. Antimicrobial activity of essential fatty acids depends on the activity of phenolic components in their content. In this study, main components in essential fatty acids was detected as thymol (%26.30), gamma-terpinene (%21.19) and benzene (%14.01). The fatty acid content of the plants varies depending on the plant type, region where it is grown and harvest time. For this reason, it is thought that thyme differs in terms of fatty acid content and antimicrobial activity in some studies (Nejad Ebrahimi et al, 2008; Imelouane et al, 2009; Satyal et al, 2016; Koçer 2021).

Table 2. Essential fatty acid components of thyme

	RT	Component	Area
1	4.95	Hexane	0.02
2	11.59	α-pinene	1.51
3	11.70	α-thujene	1.27
4	13.05	Camphene	0.49
5	14.47	Beta-pinene	0.49
6	15.92	3-Carene	0.16
7	16.29	Myrcene	1.96
8	16.50	1-Phellandrene	0.33
9	17.03	α-terpinene	3.51
10	17.71	D1-Limonene	0.61
11	18.07	Beta- Phellandrene	0.28
12	18.18	1,8-Cineole	0.45
13	18.85	1,3,6-Octatriene	0.36
14	19.58	Gamma-terpinene	21.19
15	20.34	Benzene	14.01
16	20.71	α-terpinolene	0.22
17	24.23	Ethyl amyl carbinol	0.06
18	26.04	1-Octen-3-Ol	0.58
19	26.77	Trans-sabinene hydrate	0.15
20	28.83	Camphor	0.13
21	29.17	Linalool	1.96
22	29.50	Cyclohexanol	0.14
23	29.97	2-Cyclohexen-1-ol	0.07
24	31.16	Carvacrol methyl ether	2.95
25	31.23	3-Cyclohexen-1-ol	0.99
26	31.52	Caryophyllene	3.93
27	31.80	Aromadendrene	0.16
28	33.63	α-humulene	0.33
29	33.94	3-cyclohexene-1-methanol	0.40
30	34.23	Endo-borneol	1.24
31	35.26	2-cyclohexen-1-one	0.05
32	37.58	Anethole benzene	0.06
33	38.02	Benzenemethenol	0.32
34	38.81	Carvacryl acetate	0.12

35	42.51	Caryophyllene oxide	2.33
36	44.52	Globulol	0.05
37	44.61	p-cymen-alfa-ol	0.06
38	45.54	Spathulenol	0.74
39	46.09	Eugenol	0.19
40	46.27	Carvacrol	6.05
41	47.06	Thymol	26.30
42	47.38	Dulciol C	0.09
43	49.15	1,4,7,10,13-hexaoxacyclooctadecane	0.03
44	49.41	5- α-hydroxycaryophylla	0.19

4. CONCLUSION

Thyme is a medicanal and aromatic plant rich in phenolic compounds. These components allow thyme to be used in many sectors such as medicine, food, cosmetics due to its natural content. In this study thyme showed the highest antimicrobial activity against *S.aureus* bacteria. Also, thymol was determined as the most concentrated essential fatty acid in thyme. Since there are not many studies on thyme in our country, it is thought that this study may support other studies. In future studies antimicrobial activity should be supported by minimum inhibition concentration (MIC) test, which measures the effect concentration of bacteria. In addition, there is a need for studies to determine antimicrobial activity and essential fatty acids by comparing thyme species with each other and other plants and to use these results as natural preservatives in the food industry.

REFERENCES

Bayaz, M. (2014). Esansiyel yağlar: antimikrobiyal, antioksidan ve antimutajenik aktiviteleri. *Akademik Gıda*, 12(3); 45-53.

Baydar, H. (2005). Yayla kekiği (*Origanum minutiflorum* O. Schwarz et. P. H. Davis)'nde farklı toplama zamanlarının uçucu yağ içeriği ve uçucu yağ bileşenleri üzerine etkisi. *Akdeniz Üniversitesi Ziraat Fakültesi Dergisi*, 18(2); 175-178.

Benli, M. and Yiğit, N. (2005). Ülkemizde yaygın kullanımı olan kekik bitkisinin (*Tymus vulgaris*) antimikrobiyal aktivitesi. *Orlab On-Line Mikrobiyoloji Dergisi*, 3(8); 1-8.

Borugă, O., Jianu, C., Mişcă, C., Golet, I., Gruia, A.T., Horhat, F.G. (2014). Thymus vulgaris essential oil: chemical composition and antimicrobial activity. *Journal of Medicine and Life*, Volume 7, Special Issue 3, 56-60.

Clinical and Laboratory Standards Institute (2011). Performance Standards for Antimicrobial Susceptibility Testing; Twenty-First Informational Supplement. M100-S21.

Doğan, A., Bayrak, A., Akgül, A. (1995). Bazı kekik türlerinin uçucu yağ bileşimi üzerinde araştırma. *Gıda*, 10(4); 213-217.

Ertürk, R., Çelik, C., Kaygusuz, R., Aydın, H. (2010). Ticari olarak satılan kekik ve nane uçucu yağlarının antimikrobiyal aktiviteleri. *Cumhuriyet Tıp Dergisi*, 32, 281-286.

El Hattabi, L., Talbaoui, A., Amzazi, S., Bakri, Y., Harhar, H., Josta, C., Desjobert, J.M., Tabyoui, M. 2016. Chemical composition and antimicrobial activitiy of tree essential oils from South of Morocco. *Journal of Material Environmental Science*, 7(9), 3110-3117.

Fani, M. and Kohanteb, J. (2017). In vitro antimicrobial activity of Thymus vulgaris essential oil against major oral pathogens. *Journal of Evidence-Based Complementary & Alternative Medicine*, 22(4); 660-666.

Faydaoğlu, E. and Sürücüoğlu, M.S. (2013). Tıbbi ve aromatik bitkilerin antimikrobiyal, antioksidan aktiviteleri ve kullanım olanakları. *Fen Bilimleri Enstitüsü Dergisi*, 6(2), 233-265.

Galavičová, L., Borotová, P., Valková, V., Vukovic, N.L., Vukic, M., Štefániková, J., Ďúranová, H., Kowalczewski, P.Ł., Čmiková, N., Kačániová, M. (2021). *Thymus vulgaris* essential oil and ıts biological activity. *Plants*, 10, 1959.

Gonçalves, N.D., Pena, F.L., Sartoratto, A., Derlamelina, C., Duarte, M.C.T., Antunes, A.E.C., Prata, A.S. (2017). Encapsulated thyme (*Thymus vulgaris*) essential oil used as a natural preservative in bakery product. *Food Research International*, 96, 154-160.

Imelouane, B., Amhamdi, H., Wathelet, J.P., Ankit, M., Khedid, K., El Bachiri, A. (2009). Chemical composition and antimicrobial activity of essential oil of thyme (*Thymus vulgaris*) from Eastern Morocco. *International Journal of Agrıculture & Biology*, 11, 205-208.

İlkimen, H. and Gülbandılar, A. (2018). Lavanta, ada çayı, kekik ve papatya ekstrelerinin antimikrobiyal etkilerinin araştırılması. *Türk Mikrobiyoloji Cemiyeti Dergisi*, 48(4), 241-246.

Kılıç, Ö. (2019). *Bazı bitkilerde uçucu yağların biyoaktif ve antimikrobiyal özelliklerinin araştırılması*. Ordu Üniversitesi Fen Bilimleri Enstitüsü, Yüksek Lisans Tezi, 72 sayfa, Ordu.

Koçer, O. (2021). Hatay yöresinde yetişen *Thymbra spicata L*. (Zahter/Karabaş Kekiği) bitkisinin uçucu yağ oran ve bileşenlerinin belirlenmesi. *Avrupa Bilim ve Teknoloji Dergisi*, 27,446-449.

Kürekci, C. and Sakin, F. (2017). Uçucu yağlar: antimikrobiyal açıdan uçucu yağlar: in-vitro ve in-vivo çalışmalar. *Turkiye Klinikleri*, 3(1), 15-20.

Nalbantbaşı, Z. and Gölcü, A. (2009). Kahramanmaraş yöresine ait şifalı bitkilerin antimikrobiyal aktiviteleri. *Kahramanmaraş Sütçü İmam Üniversitesi Doğa Bilimleri Dergisi*, 12(2), 1-8.

Nejad Ebrahimi, S., Hadian, J., Mirjalili, M.H., Sonboli, A., Yousefzadi, M. (2008). Essential oil composition and antibacterial activity of *Thymus caramanicus* at different phenological stages. *Food Chemistry*, 110, 927-931.

Özderin, S., Fakir, H., Dönmez, İ.E. (2014). *Muğla-Ula yöresinde doğal yayılış yapan bazı kekik türlerinin uçucu yağ oranları ve bileşenlerinin belirlenmesi*. II. Ulusal Akdeniz Orman ve Çevre Sempozyumu, 22-24 Ekim, Isparta.

Perez, A.P., Perez, N., Lozano, C.M.S., Altube, M.J., De Farias, M.A., Portugal, R.V., Buzzola, F., Morilla, M.J., Romero, E.L. (2019). The anti MRSA biofilm activity of *Thymus vulgaris* essential oil in nanovesicles. *Phytomedicine*, 57, 339-351.

Rota, M.C., Herrera, A., Martínez, R.M., Sotomayor, J.A., Jordán, M.J. (2008). Antimicrobial activity and chemical composition of *Thymus vulgaris*, Thymus zygis and *Thymus hyemalis* essential oils. *Food Control*, 19, 681-687.

Sakkas, H. and, Papadopoulou, C. 2017. Antimicrobial activity of basil, oregano and thyme essential oils. *Journal of Microbiology and Biotechnology*, 27(3), 429-438.

Satyal, P., Murray, B.L., McFeeters, R.L., Setzer, W.N. (2016). Essential oil characterization of *Thymus vulgaris* from varios geographical locations. Foods, 5(4),70.

Tural, S. and Turhan, S. 2017. Antimikrobial and antioxidant properties of thyme, rosemary, laurel essential oils and their mixtures. *Gıda*, 42(5), 588-596.

Uçar, E., Odabaş-Köse, E., Özyiğit, Y., Turgut, K. (2015). Bazı tıbbi ve aromatik bitkilerde esansiyel yağların antimikrobiyal aktivitelerinin belirlenmesi. *Süleyman Demirel Üniversitesi Ziraat Fakültesi Dergisi*, 10(2), 118-124.

Varlı, M., Hancı, H. Kalafat, G. (2020). Tıbbi ve aromatik bitkilerin üretim potansiyeli ve biyoyararlılığı. *Research Journal of Biomedical and Biotechnology*, 1, 24-32.

ÇAY YAPRAKLARINDAKİ DEĞERLİ AMİNOASİT: TEANİN

Doç. Dr. Emine NAKİLCİOĞLU [1], Selen SEYHAN [2], Eda NURKO [3]

[1] Ege Üniversitesi, Mühendislik Fakültesi, – ORCID ID: 0000-0003-4334-2900

[2] Ege Üniversitesi, Fen Bilimleri Enstitüsü,– ORCID ID: 0000-0001-6354-4687

[3] Ege Üniversitesi, Fen Bilimleri Enstitüsü, – ORCID ID: 0000-0001-9598-7407

ÖZET

Dünya'da sudan sonra en çok tüketilen içeceklerden biri çaydır. Yüzyıllardır tüketilen çay, lezzeti ve sağlığa faydalı metabolitleri sayesinde oldukça popüler hale gelmiştir. Çay, 50'den fazla ülkede yetiştirilen çay bitkilerinin (*Camellia sinensis)* kurutulmuş yapraklarından üretilmektedir. Sağlığa faydalı etkilere sahip polifenolleri, teanin, kateşin ve kafein gibi bileşikleri yapısında barındırmaktadır. Çayın en önemli metabolitlerinden biri olan teanin, çay bitkisinde doğal olarak bulunan bir aminoasittir. Öncelikle çay köklerinde sentezlenen teanin, daha sonra ksilem yoluyla çay üretimi için hasat edilen genç sürgünlere taşınmaktadır. Çay bitkisinde teanin taşınma mekanizması tam olarak bilinmemektedir. Aynı zamanda, çayın uzun mesafeli nakliyesi, hasat edilen çay yapraklarındaki teanin içeriği bakımından kritik öneme sahiptir. Bu nedenle, çay yapraklarında bulunan teanin miktarı, çay kalitesini önemli ölçüde etkilemekte ve çayın ekonomik boyutu ile ilişkilendirilmektedir. Teanin ilk olarak, 1940'lı yıllarda Sakato tarafından yeşil çay yapraklarından izole edilmiştir. Yeşil çaya ek olarak, oolong, siyah ve beyaz çayın üretildiği çay bitkisinin yapraklarında da bulunmaktadır. Yeşil çayların kuru ağırlığının yaklaşık %0.2-2.8'i ve taze çay yapraklarındaki serbest aminoasit içeriğinin yaklaşık %40-70'i teanindir. Aynı zamanda çaya umami tadı veren teanin, çayda bulunan kateşinlerin ve kafeinin acılığını ve sertliğini dengelemektedir. Özellikle rahatlatıcı etkisi bulunan bu aminoasidin, uyku kalitesi, bilişsel performans, duygusal durum, obezite, nörolojik koruma, kan basıncını düşürme, kalp-damar hastalıkları, soğuk algınlığı ve kanser üzerine olumlu etkilere sahip olduğu belirtilmektedir. Birçok fizyolojik ve farmakolojik etkiye sahip olan bu aminoasidi, gıda takviyesi veya fonksiyonel gıda bileşeni olarak kullanmaya olan ilgi gün geçtikçe artmaktadır. Bu çalışmada teaninin kimyasal yapısı, ekstraksiyonu ve sağlığa etkileriyle ilgili literatürde yer alan bilgilere değinilmiştir.

Anahtar Kelimeler: aminoasit, *Camellia sinensis*, çay bitkisi, çay, teanin

1. GİRİŞ

Çay (*Camellia sinensis*), Theaceae familyasına aittir (Alim Toraman ve Tan, 2022). Çay bitkisinin yaprakları ve tomurcuğunun işlenmesiyle elde edilen çay, Dünya'da sudan sonra en popüler olan, aromalı ve sağlıklı bir içecektir (Jiang ve ark., 2015; Yılmaz ve ark., 2016). İlk defa Çin'de rastlanılan, subtropikal ve tropikal bölgelerde yetiştirilebilen çay, Türkiye'de yalnızca Karadeniz Bölgesinde yetiştirilmektedir (Abaşin ve Duran, 2020; Alim Toraman ve Tan, 2022). *C. sinensis*'den ticari olarak kullanılabilen yeşil, siyah, beyaz ve oolong çayı üretilebilmektedir (Yılmaz ve ark., 2016; Alim Toraman ve Tan, 2022). Bu çaylar, uygulanan farklı üretim aşamaları ile ortaya çıkmaktadır (Alim Toraman ve Tan, 2022). Yeşil çay, taze çay yapraklarından işlenmeden ve fermentasyon işlemi uygulanmadan üretilirken, siyah çay işlenerek (soldurma, oksidasyon vb.) ve fermentasyon işlemi uygulanarak üretilmektedir (Yılmaz ve ark., 2016; Salman ve Özdemir, 2018). Beyaz çay, bazı genç bitki yapraklarının ve

tomurcuklarının kullanılarak, minimum işleme sonucunda üretilen çay türü iken, oolong çayı ise siyah çaydan farklı olarak kısmi oksidasyon uygulanarak elde edilen çay türüdür (Salman ve Özdemir, 2018).

Çay yapraklarının bileşimi, yetiştirildiği iklime ve genetik faktörlere göre değişiklik gösterebilmektedir (Tosun ve Karadeniz, 2005). Aynı zamanda çayların tadı ve aroması da kimyasal yapılarıyla ilişkilidir. Çay, tadı ve aroması için vazgeçilmez olan, flavonoller, flavonoidler, kateşinler, proteinler, polisakkaritler, teanin, kafein gibi daha birçok bileşiği yapısında barındırmaktadır (Jiang ve ark., 2015). Zengin kimyasal yapıya sahip olan çayın sağlığa faydalı etkileri de oldukça fazladır (Yılmaz ve ark., 2016). Bu çalışmada, çay bitkisinde bulunan teaninin kimyasal yapısı, ekstraksiyonu ve sağlığa etkileri ile ilgili literatür taraması yapılmıştır.

2. TEANİN ve KİMYASAL YAPISI

Yüzyıllardır popüler bir içecek olarak tüketilen çayın rahatlatıcı etkiye sahip olduğu ve kateşin, kafein gibi biyoaktif bileşenleri yapısında barındırdığı bilinmektedir (Türközü ve Şanlier, 2017). Sağlığa fayda sağlayan metabolitlere ek olarak, rahatlatıcı etkiden sorumlu teanin aminoasidi de son yıllarda ön plana çıkmaya başlamıştır (Dong ve ark., 2020). İlk kez 1949 yılında Sakato tarafından yeşil çay yapraklarından izole edilen bu aminoasit, 1964'den beri gıda takviyesi olarak kullanılmaktadır (Kural ve Patan, 2019). Gıda ve İlaç Dairesi (FDA) tarafından güvenli (GRAS) olarak kabul edilen teaninin, Japonya'da bitki çayları, alkolsüz içecekler ve çikolata gibi gıdalarda kullanımı onaylanmıştır (Cooper, 2012). Teanin yalnızca *Xerocomus badius* mantar türünde ve bazı çay bitkilerinin yapraklarında (*Camellia japonica, Camellia sasanqua*) bulunmaktadır (Juneja ve ark., 1999; Vuong ve ark., 2011). Çaya umami tadı veren bu aminoasit, çayda bulunan kateşin ve kafeinin acı tadını ve sertliğini dengelemektedir (Dong ve ark., 2020). Yalnızca serbest formda bulunan teanin, çay yapraklarının kuru ağırlığının %1-2'sini oluştururken, toplam serbest aminoasitlerin %40-70'ini oluşturmaktadır (Kural ve Patan, 2019; Dong ve ark., 2020). Çay yapraklarındaki teanin miktarı çayın kalitesiyle doğrudan ilişkilidir ve çayın fiyatını büyük ölçüde etkilemektedir (Vuong ve ark., 2011). Teanin miktarının siyah çayda 5.13 mg/g, yeşil çayda 6.56 mg/g, beyaz çayda 6.26 mg/g ve oolong çayda 6.09 mg/g olduğu belirtilmiştir (Barros ve Ferreira, 2017; Kural ve Patan, 2019). Çayın üretildiği coğrafi bölge, çayın türü, üretim aşamaları, hasat zamanı gibi faktörler, çaydaki teanin konsantrasyonunu etkileyebilmektedir (Türközü ve Şanlier, 2017).

γ-glutamiletilamid, y-etilamino-L-glutamik asit, y-glutamik-L-etilamit, 5-N-etilglutamin ve y-L-glu-etilamid olarak da bilinen teanin, IUPAC tarafından 2-amino-4-bütirik asit olarak adlandırılmıştır (Türközü ve Şanlier, 2017). Kimyasal formülü $C_7H_{14}N_2O_3$ ve moleküler kütlesi 174.2 g/mol'dür (Mu ve ark., 2015). Demleme esnasında çaydaki diğer bileşenlerle kimyasal reaksiyona girmeyen, renksiz, kristal bir yapıya ve iğne görünümüne sahip olan teaninin erime noktası 214–216 °C'dir (Vuong ve ark., 2011). Diğer aminoasitlerde olduğu gibi teanin de kiral karbonlara ve D-teanin ve L-teanin olmak üzere iki enantiyomere sahiptir (Mu ve ark., 2015; Kural ve Patan, 2019). Teanin, bitkilerde L-glutamik asitten sentezlenmekte ve doğada L-enantiyomer formunda bulunmaktadır (Mu ve ark, 2015). Asidik koşullarda stabil haldeyken, baz ile hidroliz edildiğinde glutamik asit ve etilamin açığa çıkmaktadır (Vuong ve ark., 2011). Kloroform, metanol ve etanol gibi çözücülerde çözünemeyen bu aminoasit, sulu ortamlarda yüksek çözünürlüğe sahiptir (Kural ve Patan, 2019).

3. ÇAYDAN TEANİNİN ELDE EDİLİŞİ ve EKSTRAKSİYON YÖNTEMLERİ

Doğal kaynaklı özlere ilgi, gün geçtikçe artmaktadır. Ürünün yüksek güvenilirliği, bitki kaynaklarına kolay erişimi ve biyoaktivitesi gibi özellikler teanin ile ilgili çalışmalara hız

kazandırmıştır. (Wang ve ark., 2012). Serbest teanin, çay bitkisinde genel olarak köklerde sentezlenir. Daha sonra bitkinin tüm kısımlarına dağılmaktadır. Teaninin özellikle çay bitkisinin yapraklarında biriktiği gözlemlenmiştir (Lin ve ark., 2022). Çayın teanin içeriği yetiştiği bölgeye, yetiştirme yöntemine, hasat zamanına ve çay türüne göre değişiklik göstermekle birlikte çaydaki teanin içeriği Vuong ve ark. (2011) tarafından ortalama %0.60-2.38 olarak tespit edilmiştir (Vuong ve ark., 2011). Çaya uygulanan soldurma ve fermantasyon işlemlerinin, teanin içeriğini %50 oranında düşürdüğü görülmüştür. Yeşil çay üretiminde bu aşamalar olmadığından teanin içeriği daha yüksek bulunmaktadır (Sarı, 2010).

Çay yapraklarında kafein ve polifenoller gibi maddelerin bulunması, teaninin yüksek saflıkta elde edilmesi konusunda zorluklar ortaya çıkarmaktadır (Vuong ve ark., 2011; Yang ve ark., 2022). Zhang ve ark. (2004), yüksek performanslı sıvı kromatografisi (HPLC) cihazı kullanarak yeşil çayda teanin tepitlenmesi üzerine çalışmışlardır. Başlangıçta kateşinler etil asetat ile ekstrakte edilmiştir. 50 ̊C'de su ile katyonik reçine kolon kullanılarak 500 g/kg teanin içeren ekstrakt elde edilmiştir. Çalışmada elde edilen teaninin saflığı %98 iken, düşük genel verim elde edilmiştir. Kolon kromatografisi kullanılarak yapılan bir çalışmada ise, Zhang ve ark. (2013), tarafından saflaştırma denemeleri gerçekleştirilmiştir. Bu çalışmada ise sıcak su ile ekstrakte edilen yeşil çayın ham özü, poliamid ve NKA-II makro gözenekli reçine kolonlarından geçirilmiştir. Sonuç olarak %96 saflıkta çay polifenolleri, %99 saflıkta teanin ve %99 saflıkta kafein elde edilmiştir. Bu metot ile teaninin geri kazanım oranı %66 olarak belirlenmiştir. Wang ve ark. (2012), yaptıkları çalışmalarında, yeşil çay ekstraktındaki polifenollerin, teaninin ve kafeinin ayrılması amacıyla sırasıyla poliamid, makro gözenekli DM-130 ve 732 katyon iyon değişim adsorbanları kullanılmıştır. Poliamid ile elde edilen kafein ve teanin fraksiyonu su ile ayrılmış, daha sonra etanol yardımıyla polifenol elde edilmiştir. Burada ayrılan kafein-teanin fraksiyonu DM 130 makro gözenekli adsorbana verilerek kafein saf olarak elde edilmiştir. Buradaki teanin fraksiyonu ise 732 katyon iyon değişim adsorbanı ile saflaştırılmıştır. Bu çalışmada %98 saflıkta teanin elde edilmiştir. Teanin miktarının belirlenmesi ve ekstraksiyon yöntemlerinin karşılaştırılması amacıyla Das ve ark. (2019), tarafından yapılan çalışmada ise, 4 farklı ekstraksiyon yöntemi (ultrasonik ekstraksiyon, çalkalamalı ekstraksiyon (agitation extraction), sıcak su ekstraksiyonu ve katı-sıvı ekstraksiyon) karşılaştırılmıştır. Ekstraktlarda teaninin tespitlenmesi için gaz kromatografisi-kütle spektrometresinden (SPME-GC-MS) faydalanılmıştır. Kolon olarak katyon değiştirici kolon tercih edilmiştir. Teanin miktarı bakımından en yüksek sonuçlar ultrasonik ekstraksiyon ve çalkalamalı ekstraksiyon yöntemlerinde sırasıyla 41,58 mg/g ve 41,61 mg/g olarak bulunmuştur. Diğer ekstraksiyon yöntemlerinde birçok nedenden dolayı teanin az miktarda tespit edilmiştir. Xu ve ark. (2020), tarafından yapılan çalışmada ise katı faz ekstraksiyonu ile HPLC cihazı kullanılarak teanin miktarının belirlenmesi üzerine çalışılmıştır. Katyon değiştirici kolon kullanılarak yapılan ekstraksiyon çalışmasında yeşil çay, sarı çay, siyah çay, beyaz çay ve oolong çayı üzerine denemeler yapılmıştır. Kullanılan yöntem ile teanin miktarı en yüksek olan çay türleri sırasıyla oolong çayı, sarı çay ve yeşil çayda olarak tespit edilmiştir.

4. SAĞLIK ETKİLERİ

Teanin aminoasidinin sağlık etkileri üzerindeki çalışmalar son yıllarda öne çıkmaktadır. Teaninin sağlık etkileriyle ilgili yapılan araştırmalar incelendiğinde rahatlama, gevşeme, bilişsel performansı ve duygusal durumu iyileştirme, kanser, kalp-damar hastalıkları, uyku kalitesi, obezite ve soğuk algınlığı üzerinde olumlu etkiler yaratma gibi özelliklere sahip olduğuyla ilgili çalışmaların bulunduğu görülmektedir (Türközü ve Şanlier, 2017; Williams ve ark., 2020)

Matsumoto ve ark. (2011), teaninin soğuk algınlığı üzerindeki etkisini incelemişlerdir. Yeşil çay ile teanin alımı sonucunda soğuk algınlığının önlenmesi amacıyla yapılan bu çalışmada, vücuda teanin alımının virüsün konakçı hücrelere adsorpsiyonunu inhibe ettiği görülmüştür. Teaninin bir miktarda olsa beyinsel fonksiyonları düzenlediği tahmin edilmektedir (Kimura, 2007). Beyinsel fonksiyonların düzenlenmesi, teaninin vücuda alındıktan sonra dopamin düzeyini arttırması ile ilişkilendirilmektedir (Müftüoğlu, 2006). Bu doğrultuda Williams ve ark. (2020), 40 kişide teanin alımının stres üzerindeki etkisini çalışmışlardır. 400 mg/gün doz alan kişilerin 200 mg/gün doz alan kişilere kıyasla nispeten stres durumlarının azaldığı belirlenmiştir. Ayrıca stres ve gevşeme etkilerine bağlı olarak uyku kalitesini de arttırdığı bilinmektedir. Jang ve ark. (2012), fareler üzerinde yaptıkları çalışmada, farelere 10 dakika arayla 22.5, 37.5, 75 ve 100 mg/kg teanin vermişlerdir. Teanin miktarı arttıkça uyku kalitesinin arttığını bildirmişlerdir. Wakabayashi ve ark. (2012), fareler üzerinde teaninin etkisi üzerine çalışmışlardır. Bu çalışma sonucunda ise, beyin kaynaklı nörotrofik faktörün indüklenmesinden kaynaklanan antidepresan semptomların gözlemlendiğini belirtilmiştir.

Birçok hastalığın temelini oluşturan obeziteye karşı ise, teaninin vücuda alımından itibaren yağ birikimini baskılama etkisinin olduğu da çalışmalarla ortaya konulmuştur (Peng ve ark., 2021). Zheng ve ark. (2005), fareler üzerinde yaptıkları çalışmada, farelere 16 hafta süre ile teanin enjekte etmişlerdir. Sonuçta ise, vücut yağ ağırlığının 16 hafta sonunda %50 azaldığı görülmüştür. Hipertansiyondan, insanlarda yaygın olarak görülen bir hastalıktır. Teaninin kan basıncını azalttığı önceki çalışmalarca ortaya konulmuştur (Nantz ve ark., 2009). Bu doğrultuda, hayvanlar üzerinde yapılan çalışmalar sonucunda, yeşil çay ve siyah çay tüketiminin teanin etkisi ile kan basıncını önemli ölçüde düşürdüğü bulunmuştur (Williams ve ark., 2019). Chen (1994), tarafından hipertansiyon hastalarında, bir yıldan fazla süreyle günlük teanin alımının kan basıncını yaklaşık olarak %20-30 aralığında azalttığı belirtilmiştir. Kanser tedavisini geliştirmek amacıyla yapılan çalışmalar ise her geçen gün artmaktadır. Kanser hastalığı kapsamında teaninin, metastazı baskıladığı ve kemoterapi tedavisini desteklediği yapılan çalışmalarca ortaya konulmuştur (Zhao ve ark., 2019). Fujii ve Inai (2008), 13 ve 78 hafta boyunca farelerin diyetlerine teanin enjekte etmişlerdir. Teaninin, fare popülasyonlarında başlangıçta görülen tümör sayısını önemli ölçüde azalttığı sonucuna varılmıştır ($p<0.05$). Sugiyama ve Sadzuka (1998), farelere tümör aşılamasından 4 gün sonra diyetlerine 10 mg/kg teanin eklemişlerdir. Yumurtalıklarda görülen tümör büyümesi, teaninin antitümör aktivitesi göstermesi ile 2.7 kat azalmıştır.

5. SONUÇ

Çay bitkilerinin yapraklarında bulunan teanin aminoasidi, fizyolojik ve farmakolojik etkileriyle son yıllarda oldukça ilgi görmeye başlamıştır. Doğal olarak sınırlı sayıda bitkisel kaynaktan elde edilen bu aminoasit, sağlığa faydalı etkileri ile biyoaktif bir bileşen olarak kabul edilebilir. Çay bitkisinin türüne, yetiştiği bölgeye, yetiştirme koşullarına, hasat yöntemine ve işleme koşullarına göre çayın teanin içeriği değişiklik gösterebilmektedir. Sentetik olarak da üretilebilen teaninin, doğal bitkisel kaynaklarına erişim oldukça kolaydır. Ancak çay yapraklarında teanine ek olarak kateşin, kafein ve polifenollerin de bulunması teanin ekstraksiyonunu zorlaştırabilmektedir. Yapılan çalışmalar incelendiğinde, yüksek saflıkta teaninin ve yüksek ekstraksiyon veriminin elde edilmesi için daha fazla çalışma yapılması gerektiği görülmektedir. Aynı zamanda teaninin başta rahatlama olmak üzere soğuk algınlığı, obezite, kalp-damar hastalıkları gibi birçok hastalık üzerine olumlu etkileri olduğu da kanıtlanmıştır. Fakat farklı form ve dozlarının sağlığa etkileri hakkında daha fazla çalışma yapılmalıdır.

6. KAYNAKÇA

Abaşin, S., Duran, Ö. Orta Asya'da çay: XVIII-XIX. yüzyıllarda bir içeceğin tarihi, Türk Tarihi Araştırmaları Dergisi, 5, 2, 2020.

Alim Toraman G. O., Tan N. Catechic tannin content of different tea samples, Journal of Advanced Research in Health Sciences, 5, 2, 2022.

Barros, L., Ferreira, I. C. Phytochemicals and their effects on human health, Curr Pharm Des, 23, 19, 2017.

Chen, Z. M. The physiologically modulating function of tea to human, Tea abstracts, 8, 1, 1994.

Cooper, R. Green tea and theanine: health benefits, International journal of food sciences and nutrition, 63, 1, 2012.

Das, P. R., Kim, Y., Hong, S. J., Eun, J. B. Profiling of volatile and non-phenolic metabolites—Amino acids, organic acids, and sugars of green tea extracts obtained by different extraction techniques, Food Chemistry, 296, 2019.

Dong, C., Li, F., Yang, T., Feng, L., Zhang, S., Li, F., ..., Zhang, Z. Theanine transporters identified in tea plants (*Camellia sinensis L.*), The Plant Journal, 101, 1, 2020.

Fujii, S., Inai, K. Tumorigenicity study of L-theanine administrated orally to mice, Food chemistry, 110, 3, 2008.

Jang, H. S., Jung, J. Y., Jang, I. S., Jang, K. H., Kim, S. H., Ha, J. H., ... Lee, M. G. L-theanine partially counteracts caffeine-induced sleep disturbances in rats, Pharmacology Biochemistry and Behavior, 101, 2, 2012.

Jiang, H., Engelhardt, U. H., Thräne, C., Maiwald, B., Stark, J. Determination of flavonol glycosides in green tea, oolong tea and black tea by UHPLC compared to HPLC, Food chemistry, 183, 2015.

Juneja, L. R., Chu, D. C., Okubo, T., Nagato, Y., Yokogoshi, H. L-theanine—a unique amino acid of green tea and its relaxation effect in humans, Trends in Food Science & Technology, 10, 6-7, 1999.

Kimura, K., Ozeki, M., Juneja, L.R., Ohira H. L-Theanine reduces psychological and physiological stress responses, Biological Psychology, 74, 2007.

Kural, B. V., Patan, H. Teanin, Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi, 8, 1, 2019.

Lin, S., Chen, Z., Chen, T., Deng, W., Wan, X., Zhang, Z. Theanine metabolism and transport in tea plants (Camellia sinensis L.): advances and perspectives, Critical Reviews in Biotechnology, 2022.

Matsumoto, K., Yamada, H., Takuma, N., Niino, H., Sagesaka, Y. M. Effects of green tea catechins and theanine on preventing influenza infection among healthcare workers: a randomized controlled trial, BMC complementary and alternative medicine, 11, 1, 2011.

Mu, W., Zhang, T., Jiang, B. An overview of biological production of L-theanine, Biotechnology advances, 33, 3-4, 2015.

Müftüoğlu, O., *Çay bir mucizedir*, Altın Kitaplar, 2016.

Nantz, M.P., Rowe, C.A., Bukowski, J.F., Percival, S.S. Standardized capsule of Camellia sinensis lowers cardiovascular risk factors in a randomized, doubleblind, placebo-controlled study, Nutrition, 25, 2009.

Peng, W. Q., Xiao, G., Li, B. Y., Guo, Y. Y., Guo, L., Tang, Q. Q. L-Theanine activates the browning of white adipose tissue through the AMPK/α-Ketoglutarate/Prdm16 axis and ameliorates diet-induced obesity in mice, Diabetes, 70, 7, 2021.

Salman, S., Özdemir, F. Beyaz çay: üretimi, bileşimi ve sağlık üzerine etkileri, Akademik Gıda, 16, 2, 2018.

Sarı, F., *Çay İşlemede Teanin Miktarının Değişimi*, Doktora Tezi, Ankara Üniversitesi Fen Bilimleri Enstitüsü, Ankara, 2010.

Sugiyama, T., Sadzuka, Y. Enhancing effects of green tea components on the antitumor activity of adriamycin against M5076 ovarian sarcoma, Cancer letters, 133, 1, 1998.

Tosun, İ., Karadeniz, B. Çay ve çay fenoliklerinin antioksidan aktivitesi, Anadolu Tarım Bilimleri Dergisi, 20, 1, 2005.

Türközü, D., Şanlier, N. L-theanine, unique amino acid of tea, and its metabolism, health effects, and safety, Critical reviews in food science and nutrition, 57, 8, 2017.

Vuong, Q. V., Bowyer, M. C., Roach, P. D. L-Theanine: properties, synthesis and isolation from tea, Journal of the Science of Food and Agriculture, 91, 11, 2011.

Wakabayashi, C., Numakawa, T., Ninomiya, M., Chiba, S., Kunugi, H. Behavioral and molecular evidence for psychotropic effects in L-theanine, Psychopharmacology, 219, 4, 2012.

Wang, L., Gong, L.H., Chen, C.J., Han, H.B., Li, H.H. "Columnchromatographic extraction and separation of polyphenols, caffeine and theanine from green tea", Food Chemistry, 131, 2012.

Williams, J. L., Everett, J. M., D'Cunha, N. M., Sergi, D., Georgousopoulou, E. N., Keegan, R. J., ..., Naumovski, N. The effects of green tea amino acid L-theanine consumption on the ability to manage stress and anxiety levels: A systematic review, Plant Foods for Human Nutrition, 75,1, 2020.

Williams, J., Sergi, D., McKune, A. J., Georgousopoulou, E. N., Mellor, D. D., Naumovski, N. The beneficial health effects of green tea amino acid l-theanine in animal models: Promises and prospects for human trials, Phytotherapy Research, 33, 3, 2019.

Xu, Y., Liu, Z., Liu, Z., Feng, Z., Zhang, L., Wan, X., Yang, X. Identification of d-amino acids in tea leaves, Food chemistry, 317, 2020.

Yang, Y., Dong, Z., Wang, Y., Xiao, F., Yang, J., Zhao, D., ..., Lu, J. Adsorption Behavior of the L-Theanine onto Cation Exchange Resin ZGSPC106Na and D001SD, Foods, 11, 22, 2022.

Yılmaz, F. T., Demirel, G., Kumsar, A. K. Çay, obezite ve kadın, Journal of Contemporary Medicine, 6, 2, 2016.

Zhang, X., Lei, S.C., Jabbar, S., Hu, B., Sun, Y. Zeng, X.X. Simultaneous separation and purification of tea bioactives from summer green tea by column chromatography, Journal of the Chemical Society of Pakistan 35, 5, 2013.

Zhang, Y., Chen, B., Huang, Z., Shi, Z. Preparative Isolation and Purification of l-Theanine by HPLC, Journal of liquid chromatography & related technologies, 27, 5, 2004.

Zhao, S., Cao, W., Xing, S., Li, L., He, Y., Hao, Z., ..., Gao, D. Enhancing effects of theanine liposomes as chemotherapeutic agents for tumor therapy, ACS Biomaterials Science & Engineering, 5, 7, 2019.

Effectiveness Of New Chemicals In The Management Of The Amount Of Apple Red Mite (*Panonychus Ulmi* Koch)

A Anorbaev[1*], A Raxmanov[2]

[1] Professor, The scientific research institute of plant quarantine and protection Tashkent, Uzbekistan

[2]**Tashkent** State Agrarian University, University str., 2, 100140 Tashkent, Uzbekistan

Abstract. The article provides information on the harm and control methods of apple red mite (*Panonychus ulmi* Koch) in apple orchards. Apple red mite (*Panonychus ulmi* Koch) is the most dangerous pest of seed orchards and other crops of other European countries. This pest can destroy more than half of the crop yield in some fields. In normal years, spiders are said to destroy 6-10% of the gross crop, and in some years even 14%. Apple red mite (*Panonychus ulmi* Koch) is the most dangerous and harmful in terms of mites. It is the main pest of melons, technical plants, and horticulture, ornamental trees. More than 150 species of spiders in the world are listed as the main pests of crops.

Materials and methods. New chemical Envidor em. k against apple red mite (*Panonychus ulmi* Koch) in seed orchards. To determine the biological effects of the drug (0.5 l / ha), research was conducted on 25 (twenty-five) hectares of Fuji apple orchards located on the territory of Zevar farm in Sariosiya district in the Surkhandarya region. Agrotoxicological experiments were carried out by the method of K.A.Gar, Sh.T.Khojaev. The calculation of biological efficacy in field and laboratory experiments was determined according to the W.S.Abbot formula, which takes into account the control option. Research results. According to research, the new Envidor em. k. (0.5 l / ha) was the highest on the 3 days of our observations in the variant in which the drug was used, i.e., the biological efficacy was 89.2%.

Conclusion. Envidor em. k. high biological efficiency can be achieved by applying the drug at the rate of consumption per hectare (0.5 l / ha). The fight against apple red mite (*Panonychus ulmi* Koch) can be obtained the expected result by timely agro-technical measures in late autumn and early spring, the use of low-toxic chemicals for the environment, and beneficial insects during the growing season.

Keywords: mite, pest, spider, drug, species, orchard, damage.

Introduction. Of the total 269.5 thousand hectares of orchards in the country, 118,000 hectares or 44% are apple orchards. Over the past 3 years, $ 750 million has been invested in horticulture. Demand for new intensive gardens is also growing [1]. Along with the expansion of seed orchards, pest infestation remains a major problem.

In orchards, several types of mites cause damage. They belong mainly to two families, the first being the four-legged mites (Tetranychidae) and the two-legged mites (Eriophyidae). These mites can be seen in the field under a special magnifying glass, in the laboratory under a microscope [2].

Several species of mites have been found to cause significant damage in seed orchards, mainly with high levels of damage. These are the gray fruit mite (*Bryobia redikorzevi* Rech), the hawthorn mite

(*Tetranychus viennensis* Zacher), the apple red canal (*Panonychus ulmi* Koch), the common spider mite (*Tetranychus urticae* Koch), and other gall-forming mites. Spider mites mainly develop and multiply under cobwebs [3].

Although several species of plant mites damage apple orchards and other crops, the most dangerous of them is the apple red mite (*Panonychus ulmi* Koch). The apple red mite is a plant-eating creature belonging to the class Arachnida, the family Acariforms [4].

Apple red mite (*Panonychus ulmi* Koch) is the most dangerous pest of seed orchards and other crops of other European countries. This pest can destroy more than half of the crop yield in some fields. In normal years, the spider kills 6-10% of the gross crop, and in some years even 14% [5,6].

In seed orchards, many species of mites, such as garden spider mite, pear mite, apple red mite, cause serious damage. Mites damage leaves, annual young twigs, growth points, and young cave fruits by sucking [7]. Damaged fruits are stained and the quality decreases. The twigs, on the other hand, lag in development and are less resistant to winter and frost.

Apple red mite (*Panonychus ulmi* Koch) is the most dangerous and harmful in terms of mites. It is the main pest of melons, technical plants, and horticulture, ornamental trees. More than 150 species of spiders have been reported as the main pests of crops around the world [8,9].

According to other scientists, the apple red mite (*Panonychus ulmi* Koch) is found in almost all agricultural areas of the world, and phytophagous mites are more plant-related than all other mites [10]. Spiders were found to infect 1,200 species of cultivated and other plants, and 150 of these plants were found to be at high economic risk [11,12].

Materials and methods: New chemical Envidor em. k against apple red mite (*Panonychus ulmi* Koch) in apple orchards. To determine the biological effects of the drug (0.5 l / ha), research was conducted on 25 (twenty-five) hectares of Fuji apple orchards located on the territory of the farm "Zevar" Sariosiya district of Surkhandarya region. According to him, to test chemicals envidor em. k. (0.5 l / ha) of the active substance (spiridiclofen).

As a standard for this drug, Error received 1.8% em. k. (0.4 l / ha) of the active substance (abamectin). Because both of these drugs are recommended for mites in other crops. They researched to determine their biological efficacy by mutual comparison.

The research is carried out using widely used methods and techniques for the detection of agricultural pests. Entomological calculations and observations were performed using G.Ya. Bey Beyenko, L.A. Kopaneva detectors; K. Fasulati's methods in determining the density, occurrence, dominants of pests; performed based on. The degree of pest infestation was determined by the method of VI Tansky. Agrotoxicological experiments. K.A.Gar methodical manuals, W.Abbott's formula, and Sh.T.Khodjaev's methodical instructions were carried out. sprinkled at the expense of the working fluid. In large field experiments using special centralized sprayers, 1000 l / ha. The working fluid was applied

sparingly. The effect of chemical drugs on entomophagous was studied by the method of B.B. Adashkevich et al. (1983).

1 **2**

1-2 figure. Accounting for the eggs of apple red mite (*Panonychus ulmi* Koch)

Results and discussion: Apple red mite (*Panonychus ulmi* Koch) is considered to be the dominant species of mites in apple orchards. The biological effectiveness of this antiviral drug Envidor em. k reached 100% when applied to 0.4-0.6 l / ha in the presence of 5.3-6.7 mobile apple red mites per leaf. In 2017, experiments were conducted in the Texron region on the Golden delicious variety of apples with the drug Envidor em. k (0.5 l / ha) against apple red mite.

Observations were made on days 3, 7, 14, and 21 to determine the effect of the Envidor em. k drug (0.5 l / ha) applied against apple red mite (*Panonychus ulm*i Koch). The Henderson-Tilton formula was used to determine the number of apple red mites (*Panonychus ulmi* Koch) on a single leaf. The results of the study showed that after administration of the Envidor em. k drug (0.5 l / ha), the biological efficacy increased by 82% by day 14 [11].

Experiments have been carried out in Polish apple orchards to control apple red mites (*Panonychus ulmi* Koch). The Envidor em. k drug was applied to the consumption of apple trees before flowering (03-0.4 l / ha). Experiments have shown that when Envidor em. k is used in the fight against apple red mite (*Panonychus ulmi* Koch), the duration of action is 2-6 weeks [13].

Envidor em. k drug (spirodiclofen), one of the acaricides with a new method of action, was applied to the eggs of apple red mites (*Panonychus ulmi* Koch) in 2004-2008. The experiments were conducted on apple orchards in Serbia, according to which the biological efficiency was 89-86% [14].

Endor drug apple red mites (*Panonychus ulmi* Koch) has a strong effect on the biosynthetic properties of lipids, used in apple orchards during the ovarian, larval, and nymph periods, the laying of eggs by female mites. This drug can achieve the expected results when applied to apple orchards during flowering and fruit development [15,16].

Apple red mites (*Panonychus ulmi* Koch) can be applied to the eggs envision in the consumption brain (03-0.4 l / ha) at a temperature of 5 ºC to 25 ºC.

According to our research, in apple orchards, the apple red mite (*Panonychus ulmi* Koch) is infested with eggs, larvae, and nymphs by Envidor em. k. (0.5 l / ha) was used.

As a benchmark for this drug, Error used 1.8% em. k. (0.4 l / ha) was obtained. Control observations were analyzed from 3 days of use of the drugs obtained for the experiment. Before processing, Envidor em. k. (0.5 l / ha) in the variant in which the drug was used, an average of 6.8 units per leaf, Error 1.8% em. k. (In the variant applied to 0.4 l / ha, it was 7.2 units.

Table 1.

Envidor em. k. against apple red mite (*Panonychus ulmi* Koch). (0.5 l / ha) Biological efficacy of the drug 15.08.2019 y

Options	Consumption rate l / ha	Number of pests per leaf, pcs					Biological efficiency,%, by days			
		Pre-processing number	The number after processing, pcs							
			3	7	14	21	3	7	14	21
Envidor em. k.	0,5	6,8	0,9	1,6	2,7	3,4	**89,2**	82,8	74,1	69,0
Errou 1.8% em.k	0,4	7,2	1,2	2,0	3,1	3,7	**86,4**	79,8	72,1	68,6
Control	-	8,3	10,2	11,4	12,8	13,6	-	-	-	-

According to research, the new Envidor em. k. (0.5 l / ha) in the variant in which the drug was administered, our observations were highest on the 3rd day after drug administration, i.e., the biological efficacy was 89.2%, and on the 7th day, it was 82.8%. By the 14th day of our observations, the biological efficiency was 74.1%, and on the 21st day, it was 69.0%. From the 21st day of the study, the number of pests began to increase again. (Table 1)

In our variant using the following template, Error has a 1.8% em. k. (0.4 l / ha) was highest on the next 3 days of treatment, i.e., the biological efficiency was 86.4%, while on the 7th day the biological efficiency was 79.8%. By the 14th day of our observations, the biological efficiency was 72.1%, while on the 21st it was 68.6%. In this variant, too, the biological efficacy index was found to decrease after 21 days. It was observed that the chemical effect on the eggs and nymphs of the pest was low.

Conclusions: According to the results of the study, timely control of apple red mite (*Panonychus ulmi* Koch) in orchards is an important factor in their control, taking into account its bioecology and survival, using effective mites. Envidor em. k. high biological efficiency can be achieved by applying the drug at the rate of consumption per hectare (0.5 l / ha). In the fight against apple red mite (*Panonychus ulmi* Koch) in apple orchards can be maintained crop in late autumn and early spring by timely agro-technical measures, the use of low-toxic chemicals for the environment, and beneficial insects during the growing season.

References

[1] H.Kimsanboyev, S.Ergashev, R.O'lmasboyeva B S *Entomology* (2006)

[2] Xo`jaev Shomil Tursunovich *Fundamentals of entomology, crop protection and agrotoxicology* (2014)

[3] Harris A L, Ullah R and Fountain M T 2017 The evaluation of extraction techniques for Tetranychus *Exp. Appl. Acarol.* **72** 367–77

[4] Balykina E B, Rybareva T S and Yagodinskaya L P 2021 Population of tetranychidae mites on apple trees and methods of restraining the number of resistant races in crimea *E3S Web of Conferences*

[5] Petrović A, Ivanović I, Manojlović A, Banjac B, Malenčić Đ, Marinković D and Bursić V 2021 Factors and mechanisms of acaricide resistance in European red mite (Panonychus ulmi Koch) *Biljn. Lek.* **49** 626–44

[6] Bittencourt L, Fauvel G and Orts r influência do estresse hídrico sobre a fisiologia de macieiras e a flutuação de Panonychus ulmi (ACARI : TETRANYCHIDAE) Influence of water stress on the phisiology of apple trees and on the 97–106

[7] Yorulmaz Salman S and Keskin C 2019 Contact toxicity of pine, laurel and juniper essential oils to spirodiclofen-resistant and -susceptible Tetranychus urticae Koch, 1836 (Acari: Tetranychidae) populations *Turkiye Entomoloji Derg.* **43** 97–105

[8] Gräff C, Johann L, Souza C and Ferla N 2017 Patogenicidade de Isaria fumosorosea sobre o ácaro vermelho europeu em laboratório. *Biotemas* **30** 73–8

[9] Marcic D, Ogurlic I, Prijovic M and Peric P 2009 Effectiveness of azadirachtin (NeemAzal-T/S) in controlling pear psylla (Cacopsylla pyri) and European red mite (Panonychus ulmi)

Pestic. i fitomedicina **24** 123–31

[10] Kramer T and Nauen R 2011 Monitoring of spirodiclofen susceptibility in field populations of European red mites, Panonychus ulmi (Koch) (Acari: Tetranychidae), and the cross-resistance pattern of a laboratory-selected strain *Pest Manag. Sci.*

[11] Badieinia F, Khajehali J, Nauen R, Dermauw W and Van Leeuwen T 2020 Metabolic mechanisms of resistance to spirodiclofen and spiromesifen in Iranian populations of Panonychus ulmi *Crop Prot.*

[12] Khamis M and Khalil S 2019 Article History Comparative toxicity study of different acaricides in laboratory preluding for field efficacy assessment against Tetranychus urticae (Acari: Tetranychidae) *J. Plant Prot. Res. Inst* **2** 576–85

[13] Auger P, Bonafos R, Guichou S and Kreiter S 2003 Resistance to fenazaquin and tebufenpyrad in Panonychus ulmi Koch (Acari: Tetranychidae) populations from South of France apple orchards *Crop Prot.* **22** 1039–44

[14] Zhou Y, Jia H, Zhou X, Cui Y and Qian J 2018 Epidemiology of spider mite sensitivity: A meta-analysis and systematic review *Clin. Transl. Allergy* **8** 1–10

[15] Joshi N K, Leslie T, Rajotte E G and Biddinger D J 2020 Environmental impacts of reduced-risk and conventional pesticide programs differ in commercial apple orchards, but similarly influence pollinator community *Chemosphere* **240** 124926

[16] Koo H N, Choi J, Shin E, Kang W, Cho S R, Kim H, Park B and Kim G H 2021 Susceptibility to acaricides and the frequencies of point mutations in etoxazole- and pyridaben-resistant strains and field populations of the two-spotted spider mite, tetranychus urticae (Acari: Tetranychidae) *Insects* **12**

Gümüş Nitrat ve Gümüş Nanopartiküllerin *Salvia officinalis* Bitkisinde Rosmarinik Asit ve Kafeik Asit İçeriğine Etkisi

NİHAL BALTACI [1], SEMİHA ERİŞEN [2]

[1] YILDIZ TEKNİK Üniversitesi, Fen Edebiyat Fakültesi, - 0000-0003-2851-1489

[2] YILDIZ TEKNİK Üniversitesi, Fen Edebiyat Fakültesi, - 0000-0002-0542-5118

ÖZET

Lamiaceae/Labiatae familyasının Salvia cinsine ait olan *Salvia officinalis* ekonomik değeri olan tıbbi ve aromatik bir bitkidir. Türkiye'de 'adaçayı', 'diş otu' veya 'meryemiye' olarak da bilinen *S. Officinalis,* başta rosmarinik asit ve kafeik asit olmak üzere değerli sekonder metabolit içeriğine sahiptir. Günümüzde tıbbi kullanımının yanı sıra endüstride gıda, kozmetik gibi sektörler için önemlidir ve yetiştiriciliği en çok yapılan Salvia türüdür. Değerli metabolitlerin üretiminde elisitör uygulamaları in vivo ve in vitro çalışmalarda oldukça yaygındır ve elisitör olarak metal iyon ve nanopartiküllerin bitkilere uygulanması önemli metabolitlerin miktarlarında artışa yol açmaktadır. Bu çalışmada gümüş nitrat ($AgNO_3$) ve gümüş nanopartiküllerin (AgNP) *S. officinalis* bitkisinde önemli sekonder metabolitler olan rosmarinik asit ve kafeik asit miktarına etkisi incelenmiştir. Bu amaçla bitki büyütme odasında 3:1 torf/perlit içeren saksılarda yetiştirilen 3 aylık (10-12 yapraklı) bitkilere yapraktan spreyleme yöntemiyle 50 mg/l $AgNO_3$ veya AgNP içeren deiyonize su uygulanmış, bitkiler uygulamadan sonra iki farklı zamanda (7. ve 15. gün) hasat edilmiştir. Hasat edilen yapraklar kurutulduktan sonra hazırlanan metanol ekstraktları yüksek performanslı sıvı kromatografisi (HPLC) ile analiz edilmiştir. Elde edilen veriler değerlendirildiğinde; $AgNO_3$ ve AgNP uygulaması yapılan bitkilerde kontrol bitkilerine oranla rosmarinik ve kafeik asit miktarlarının anlamlı şekilde arttığı istatistiksel olarak tespit edilmiştir. Rosmarinik asit içeriği açısından en iyi değer, $AgNO_3$ uygulaması sonrası 7. günde hasat edilen bitkilerde 25,95 (mg/g DW) olarak, kafeik asit için ise en iyi değer, AgNP uygulaması sonrası 7. günde hasat edilen bitkilerde 1,22 (mg/g DW) olarak elde edilmiştir. Uygulamadan 15 gün sonra hasat edilen bitkilerde hem rosmarinik asit hem de kafeik asit miktarı için en yüksek değer $AgNO_3$ uygulaması sonrası sırasıyla 10,96 (mg/g DW) ve 0,81 (mg/g DW) olarak belirlenmiştir.

Anahtar Kelimeler : Sekonder metabolit, adaçayı, gümüş nitrat, gümüş nanopartikül, rosmarinik asit, kafeik asit

ASSESSMENT OF METAL LEVELS IN TEA

ABOUREJAL Nesrine
Université ABOU BEKR BELKAID, Tlemcen ALGERIE
ORCID ID 0000-0003-4100-2865
BENAMARA Salim
Université ABOU BEKR BELKAID, Tlemcen ALGERIE
HADJ MIMOUNE Khadidja
Université ABOU BEKR BELKAID, Tlemcen ALGERIE khadidja. Hadj
GHORZI Ikram
Université ABOU BEKR BELKAID, Tlemcen ALGERIE

Abstract
Food consumption is the most likely route of human exposure to metals. Tea (Camellia sinensis L.) is among the most widely consumed non-alcoholic beverages. The objective of our study is to estimate the levels of four metals in tea infusions in order to assess the risk to human health. This is a cross-sectional study for analytical purposes made on 8 brands of tea sold on the Algerian's markets. Four metal contaminants (Pb, Cd, Cu, Zn) were analyzed by polarography. The results revealed that the average concentrations were in the following order: Zn> Cu> Pb> Cd in all samples with levels of 69.42, 32.47, 0.91, 0.05 respectively without exceeding the permissible value stipulated by the world health organization (WHO). We noted an increase in the levels of metals in the infusions over time but without significant difference. However, a significant difference (p) was observed between the different brands and the level of lead according to the different infusion times. The Hazard Quotient (HQ) and Hazard Index (HI) levels of tea were all below 1, making it safe to consume tea infusions against these four contaminants.

Keywords: tea, infusion, metals, HQ and HI

YUMURTA KABUĞU ATIĞININ DEĞERLENDİRİLMESİ

Doç. Dr. Emine NAKİLCİOĞLU [1], Dr. Ceyda DADALI [2], Gizem TİRYAKİ [3]

[1] Ege Üniversitesi, Mühendislik Fakültesi, emine.nakilcioglu@ege.edu.tr - https://orcid.org/0000-0003-4334-2900
[2] Ege Üniversitesi, Mühendislik Fakültesi, ceyda.dadali@ege.edu.tr - https://orcid.org/0000-0003-2102-8582
[3] Ege Üniversitesi, Mühendislik Fakültesi, gizemmtiryaki@gmail.com - https://orcid.org/0000-0001-5608-9815

ÖZET

Yumurta sağlığa olan faydaları ve besleyici içeriği ile bilinen doğal bir besindir. Günümüzde sıklıkla tüketilen yumurtanın kabuğu ve zarı; tüm yumurtanın yaklaşık %11'ini oluşturan önemli bir atıktır. Bu tür atıklarla ilgili en önemli zorluk çevresel etkidir. Organik ve inorganik bileşikler açısından zengin olan yumurta kabuğu atıklarının gıda sanayiinde ve daha birçok endüstriyel alanda kullanılarak değerlendirilmesi sonucunda, çevreye ve ülke ekonomisine katkı sağlanabilir. Yapılan çalışmalarda yumurta kabuğu atığının gıda takviyesi olarak kullanılabilir bir kalsiyum kaynağına dönüştürülme potansiyeli olduğu görülmektedir. Ayrıca yumurta kabuğunun kek, yoğurt, sosis, bisküvi ve kahve gibi gıda ürünlerini zenginleştirmek için kullanılabileceği görülmektedir. Bunun dışında yumurta kabuğunun ilaç ve tarım gibi diğer alanlardaki potansiyel uygulamaları da tartışılmaktadır. Yem ve gübre üretimi, toprak iyileştirici gibi farklı alanlarda kullanılabilen değerli bir materyal olan yumurta kabuğu, çevre dostu bir katalizör olarak kullanılması gibi ilginç özellikler sunmaktadır. Yumurta kabuklarından elde edilen atıkların tıbbi cerrahide kullanılan biyomateryallere dönüştürülmesi, atık kullanımına daha fazla değer katacak bir stratejidir. Son yıllarda yumurta kabuğundan türetilmiş parçacıklara sahip yapısal kompozitlerin mekanik özellikleri, polimer, metal ve seramik matris malzemeleri için tartışılmaktadır. Yumurta kabuğu atığının yeni kullanımların bulunması biyoekonomi topluluğu için büyük bir fırsattır. Yumurta kabuğundan maliyeti düşük, biyoyararlılığı yüksek ve çevre açısından güvenli bir biçimde kalsiyum eldesi mümkündür. Yapılan çalışmalarda önerilen tüm ürünler ve süreçler yüksek ekonomik, sağlık ve çevresel faydalar sunmaktadır. Bu çalışmada gıda sanayisinin önemli bir atığı olarak karşımıza çıkan yumurta kabuğunun, katma değerli ürünler haline dönüştürülmesiyle ilgili literatür verileri sunulmaktadır.

Anahtar Kelimeler: atık, atık değerlendirme, kalsiyum, yumurta kabuğu.

1. GİRİŞ

Yumurta kabuğu, yumurtayı dış etkilerden koruyan, büyük çoğunluğu (%97) kalsiyum karbonattan ($CaCO_3$) oluşan ve yumurtaya şeklini veren kısımdır. Yumurta kabuğu gelişmekte olan embriyo için mekanik koruma, kontrollü bir gaz değişimi ve başta kalsiyum olmak üzere

birçok besin kaynağı sağladığından önemli bir yapıdadır [1]. Kabuk, yumurtanın bakteri, virüs ve diğer patojenlerin kontaminasyonunu önleyerek arındırılmış bir şekilde tüketiciye ulaşmasını sağlamaktadır. Sağlığa olumlu etkileri bulunan yumurta kabuğu güçlü kalsiyum takviyesi olup diş sağlığını korumaktadır. Yapısında bulunan vitamin ve mineraller sayesinde cilt hücrelerini yenileyerek ciltte oluşan tahrişi iyileştirmektedir. Bunların dışında yapısındaki protein ve kalsiyum sayesinde kemik erimesini önlemektedir [2].

Dünya çapında yılda yaklaşık 65,5 milyon ton yumurta üretilmektedir. Tavuk yumurtalarının dünya çapında daha fazla tüketilmesi ve kullanılması, başta yumurta kabuğu olmak üzere artan miktarda yumurta atığına neden olmaktadır. Bu atık ürünlerin bertarafındaki en önemli zorluk, çevresel etkidir. Yumurta kabuğu atıkları genellikle düzenli depolama alanlarına atılır ve bu nedenle koku üretimi ve mikrobiyal gelişim ile bir kirlilik kaynağı haline gelmektedir. Bu zorluğu çözmek için, özellikle yumurta kabuğu atığı Avrupa Birliği yönetmeliklerine göre tehlikeli bir atık olarak kabul edildiğinden, gıda atığı arıtımına yönelik optimum stratejilerin geliştirilmesi gerekmektedir. Endüstriyel işlemlerden kaynaklanan yumurta kabuğu atıkları, toprak pH'ını artırmak için bir ajan olarak tarımda kullanılabilmektedir [3]. Aynı zamanda, yumurta kabuğu atığının gıda takviyesi olarak biyoyararlılığı yüksek bir kalsiyum kaynağına dönüştürülme potansiyeli hakkında çalışmalar yapılmıştır [4]. Elde edilen bulgular ve sonuçlar incelendiğinde yumurta kabuğunun kek, yoğurt, sosis, bisküvi ve kahve gibi gıda ürünlerini zenginleştirmek için kullanılabileceği görülmektedir.

2. YUMURTA KABUĞUNUN YAPISINDAKİ KALSİYUM

2.1. İNSAN SAĞLIĞI İÇİN KALSİYUM

Diyette kalsiyum (Ca) eksikliği yaygın bir sorundur. Süt ürünlerinden kalsiyum alımı, kalsiyum gereksinimlerini karşılamanın uygun bir yoludur. Ancak, genellikle insanlar bunları belirlenen miktarlarda tüketmezler. Tavuk yumurtası kabuğu, evde bulunan ve kalsiyum takviyesi olarak kullanılabilecek bir kalsiyum kaynağıdır. Kalsiyum, çeşitli fizyolojik işlevler ve yaşam boyunca kemik dokularının bakımı için insan vücut sağlığı açısından gerekli bir mineraldir. Sinir iletimi, kas kasılması, hücre yapışması, mitoz, kan pıhtılaşması ve iskeletin yapısal desteği gibi kritik biyolojik fonksiyonlar için gerekli olan temel bir mineraldir [5]. Son yıllarda, yeterli kalsiyum alımının osteoporoz, hipertansiyon ve kolon kanseri gibi kronik hastalıkların yanı sıra bir dizi başka hastalık riskini azalttığı gösterilmiştir. Özellikle kemik demineralizasyonunun tedavisinde ve önlenmesinde önemli bir rol oynamaktadır [6].

Kalsiyum içeriği %38’ e varan tavuk yumurta kabuğu tozu, insan beslenmesi için umut verici ancak az bilinen bir kalsiyum kaynağıdır. Yumurta kabuğu tozu kullanımı, osteoporozlu hastalarda kemik yoğunluğunu arttırmakta ve ağrıyı azaltmaktadır. Yumurta kabuğu iyi bir doğal kalsiyum kaynağıdır ve yaklaşık %90 oranında emilebilmektedir [7].

2.2. YUMURTA KABUĞUNUN KALSİYUM KAYNAĞI OLARAK DEĞERLENDİRİLMESİ

Dünyanın birçok ülkesinde yumurta kullanan gıda üreticileri tarafından tonlarca yumurta kabuğu, atık olarak üretmektedir ve bu da ciddi bir çevre sorununa neden olmaktadır. Birçok araştırmacı yumurta kabuğunu, insan beslenmesinde kalsiyum kaynağı olarak kullanmanın yollarını aramaktadır. Bu sayede, bu atıklar değerlendirilerek, günlük kalsiyum alımını arttırılacaktır. Yumurta kabuğu toplam yumurta ağırlığının %9-12'sini oluşturmakta ve büyük ölçüde kalsiyum karbonattan (%94) ve organik matris üzerinde bir miktar magnezyum karbonat ve kalsiyum fosfattan oluşmaktadır (Çizelge 1). Yumurta kabuğu kalsiyumu iyi bir diyet kalsiyum kaynağıdır ve mükemmel bir ikame malzemesidir.

Çizelge 1. Yumurta kabuğunun besinsel bileşimi [7]

	Beyaz yumurta kabuğu tozu	Kahverengi yumurta kabuğu tozu
Nem (%)	0,46	0,20
Protein (%)	3,92	5,04
Kül (%)	94,61	94,28
Yağ	0,35	0,08
Kalsiyum (%)	34,12	33,13
Magnezyum (%)	0,29	0,36
Fosfor (%)	0,04	0,07
Potasyum (%)	0,03	0,04
Sodyum (%)	0,05	0,04
Bakır (ppm)	< 1 ppm	< 1 ppm
Demir (ppm)	22 ppm	< 1 ppm
Manganez (ppm)	< 1 ppm	< 1 ppm
Çinko (ppm)	< 1 ppm	< 1 ppm

3. YUMURTA KABUĞUNUN DEĞERLENDİRİLMESİYLE İLGİLİ ÇALIŞMALAR

Yumurta kabuğu kullanılarak yapılan çalışmalarda atıkların karakterizasyonu üzerine çalışılmıştır. Yumurta kabuğu atıklarının gıda formülasyonlarında kullanımıyla ilgili olarak ise sınırlı sayıda çalışma bulunmaktadır. Hassan (2015), yumurta kabuğunu doğrudan bisküvi karışımına ekleyerek kalsiyum içeriğinde artış gözlemlemiştir. Ray vd. (2017), çikolatalı keke yumurta kabuğu tozu ekleyerek dokusal ve duyusal özelliklerde oldukça az değişiklikler gözlemlemişlerdir. Kobu-Cisowska vd. (2020), Polonya ekmeğine %0,27 oranında yumurta kabuğu ekleyerek fırınlamış ve kalsiyum seviyesini 2,5 kat arttırmıştır. Novelina vd. (2020), %0,8 oranında yumurta kabuğu tozunu soya sütü jöle şekerine ekleyerek %0,51 oranı ile optimum miktarda kalsiyum içeriği elde etmiştir. Lachowicz vd. (2020), aronya ve kızılcık suyuna %2 oranında yumurta kabuğu tozu ilave ederek %1 oranında yumurta kabuğu tozunun optimum olduğunu gözlemlemiştir. Platon vd. (2020), yumurta kabuğu tozunu ekmek tarifine eklemiştir. Cho vd. (2017) yaptıkları bir çalışmada domuz ürünlerinde sentetik fosfat ikame maddeleri olarak istiridye kabuğu ve yumurta kabuğunun optimum oranını belirlemeyi amaçlamıştır. Adal (2018) yaptığı çalışmada kalsiyum kaynağı olarak yumurta kabuğu tozu ilave edilerek hazırlanan hamur ve ekmeklerin fiziksel, kimyasal, reolojik ve duyusal özelliklerini belirlemiştir. Zerek (2021) ise yumurta kabuğu atıklarının geri kazanımını sağlamak için %0, %3, %6 ve %9 oranında yumurta kabuğu tozu eklenmiş kurabiyelerin besin değerini ve duyusal özelliklerini incelemiştir. Afzal vd. (2020), geliştirilmiş duyusal özelliklere

sahip çörek için yumurta kabuğu tozu ekleyerek kalsiyum içeriğinde önemli bir artış gözlemlemiştir.

4. SONUÇ

Küresel ölçekte artan yumurta üretimi ve dolayısıyla artan yumurta kabuğu atıkları çevresel açıdan sorun teşkil etmektedir. Yumurta kabuğunda yer alan zengin kalsiyum miktarı ve insan tüketimi için faydalı olan diğer mineraller göz önüne alındığında, yumurta kabuğunun çeşitli tarımsal, tıbbi ve endüstriyel uygulamalarda kullanılabiliyor olmasının yanı sıra gıda sanayiinde değerlendirilmesi de önem arz etmektedir. Yumurta kabuğunun geri dönüşümü hem çevreye hem de tüketicilere oldukça fayda sağlamaktadır. Böylece yumurta kabuklarının çöpe atılmasından kaynaklanan sera gazı üretiminin azaltılarak çevrenin korunması hedeflenmektedir. Kalsiyum eksikliğinin hızla arttığı mevcut durum düşünüldüğünde de tüketiciler için kalsiyumca zenginleştirilmiş yeni gıdaların geliştirilmesi son derece önemli hale gelmektedir. Buna ek olarak, yumurta kabukları ilaç endüstrisi, hayvan yemi ve toprak zenginleştirici gibi diğer çeşitli alanlarda da kullanılabilmektedir. Tıbbi uygulamalarda kullanılan biyomalzemelerin üretimine de önemli katkı sağlamaktadır. Yumurta kabuklarının değerlendirilmesi ekonomik, çevresel ve sağlık açısından birçok fayda sağlaması sebebiyle, hakkında daha çok araştırma ve çalışma yapılarak gelişmelerin gözlenmesine ihtiyaç duyulmaktadır.

KAYNAKÇA

[1] Hunton, P. (2005). Research on Eggshell Structure and Quality: an Historical Overview. Brazilian Journal of Poultry Science, 7, 67-71.

[2] Oliveira, D. A., Benelli, P., & Amante, E. R. (2013). A Literature Review on Adding Value to Solid Residues: Egg Shells. Journal of Cleaner Production, 46, 42-47.

[3] Vandeginste, V. (2021). Food Waste Eggshell Valorization Through Development of New Composites: A Review. Sustainable Materials and Technologies, 29, E00317.

[4] Aditya, S., Stephen, J., & Radhakrishnan, M. (2021). Utilization Of Eggshell Waste in Calcium-Fortified Foods and Other İndustrial Applications: a Review. Trends in Food Science & Technology, 115, 422-432.

[5] Miller, G. D., & Anderson, J. J. (1999). The Role of Calcium in Prevention of Chronic Diseases. Journal of The American College of Nutrition, 18(Sup5), 371S-372S.

[6] Miller, G. D., Jarvis, J. K., & Mcbean, L. D., *Additional Nutrients and Bone Health*, Handbook of Dairy Foods and Nutrition, CRC Press, 2006.

[7] Ray, S., Barman, A. K., Roy, P. K., & Singh, B. K. (2017). Chicken Eggshell Powder as Dietary Calcium Source in Chocolate Cakes. The Pharma Innovation, 6(9, Part A), 1.

INVESTIGATION OF BLOOD GAS PARAMETERS IN SHEEP WITH TORSION UTERI

Dr. Öğr. Üyesi Tarık ŞAFAK

Kastamonu University, Faculty of Veterinary Medicine, Department of Obstetrics and Gynecology, tsafak@kastamonu.edu.tr - https://orcid.org/0000-0002-6178-4641

ABSTRACT

In this study, it was aimed to investigate the blood gas parameters in sheep with uterine torsion. The study was conducted on three groups: dystocia group due to uterine torsion (UT) (n: 14), dystocia group other than torsio (OD) (n: 10), and sheep with normal vaginal delivery (VD) (n: 7). All sheep had blood drawn from their jugular veins. In both the UT and OD groups, the sample time was right before the cesarean section or delivery assistance. However, in the VD group, blood samples were collected within an hour after the delivery. Venous pH, pCO_2, Na^+, K^+, Cl^-, iCa^{+2}, HCO^{3-}, anion gap values in blood samples were measured with ABL80 FLEX radiometer blood gas analyzer. While HCO3- (28.3 mmol/L) (P = 0.001) and anion gap (32.3 mmol/L) (P < 0.001) concentrations were found to be high in TG, the Cl- (99 mmol/L) (P < 0.001) concentration was found to be low. Venous pH (7.42) (P=0.002) and Na^+ concentration (146 mmol/L) (P = 0.001) were low in VD, but pCO2 (38.0 mmHg) (P = 0.002) and K^+ (4.39 mmol/L) (P = 0.01) concentrations were found to be high. There was no statistical difference between the groups in the iCa^{+2} concentration. As a result, hemodynamic balances in torsio uteri instances in sheep deteriorate. It was found that these characteristics should be considered when performing fluid treatment in dystocia.

Keywords: Sheep, Dystocia, Torsio uteri, Blood gas analysis

NERVÖZ DİSTEMPERLİ BİR KÖPEKTE BEYİN OMURİLİK SIVISI ANALİZ BULGULARI

Dr. Öğr. Üyesi Şükrü DEĞİRMENÇAY[1], Arş. Gör. Emre EREN[2], Dr. Öğr. Üyesi Sıtkıcan OKUR[3]

[1] Atatürk Üniversitesi Veteriner Fakültesi İç Hastalıkları ABD, s.değirmencay@atauni.edu.tr - 0000-0002-3920-6343

[2] Atatürk Üniversitesi Veteriner Fakültesi İç Hastalıkları ABD, emreeren@atauni.edu.tr- 0000-0003-3118-7384

[3] Atatürk Üniversitesi Veteriner Fakültesi İç Hastalıkları ABD, sitkican.okur@atauni.edu.tr- 0000-0003-2620-897X

ÖZET

Bu vaka raporunda nervöz distemper tanısı konulan bir köpekte beyin omurilik sıvısı (BOS)'nın hematolojik ve biyokimyasal analiz bulgularını bildirmek amaçlandı. Olgu materyalini, istemsiz kasılmalar, mukopurulent göz yaşı ve burun akıntısı ve halsizlik şikayetlerine sahip 8 aylık, 20 kg canlı ağırlığında, dişi, kısırlaştırılmamış kangal ırkı bir köpek oluşturdu. Yapılan klinik muayenede mukopurulent gözyaşı ve burun akıntısı, 40,1 °C rektal sıcaklık, ön ve arka bacak kaslarında myoclonus tespit edildi. Gözyaşı ve burun akıntısı örneklerinde yapılan hızlı tanı test kiti sonuçlarında canine distemper virüs (CDV) antijeni saptanırken canine influenza ve canine adenovirus tip 2 antijeni saptanmadı. Hematolojik ve biyokimyasal analizler için alınan venöz kan örneklerinde nötrofilik lökositosis ($14,72x10^9$/L) saptanırken, kreatinin kinaz-myokardiyal band (CK-MB) (214 U/L) ve laktat dehidrogenaz (LDH) (481 U/L) seviyelerinde yükselme saptandı. Total protein (TP) (4,84 g/dL) seviyesi azalırken albümin (ALB) (2,90 g/dL) ve glikoz (86 mg/dL) düzeyleri referans değerler arasındaydı. Anesteziye alınan köpekten 22 gauge'lik spinal iğne ile serebellomedüller sisternal aralıktan ponksiyon yöntemi ile BOS örneği alındı. BOS örneğinde yüksek TP (2 g/dL) ve ALB (1 g/dL) düzeyleri saptandı ve glukoz düzeyi 55 mg/dL olarak bulundu. Ancak bu değerlerin kan serum düzeylerinden daha düşük olduğu saptandı. Yüksek bir albumin quota (AQ) oranı (34.48) mevcuttu. Sonuç olarak sinirsel bulguların yeni başladığı nervöz distemper vakalarında CDV enfeksiyonu kaynaklı kan beyin bariyeri bütünlüğünün bozulması BOS örneğinde TP ve ALB düzeylerinde yükselme ile sonuçlanır. BOS örneğinde kan serum düzeylerinden daha düşük TP ve ALB düzeylerinin saptanmasının sinirsel bulguların yeni başlamasına bağlı olduğu ve bu durumun prognostik bir gösterge olarak kullanılabileceği düşünüldü.

Anahtar Kelimeler: beyin omurilik sıvısı analizi, nervöz distemper

ANALYSIS FINDINGS OF CEREBROSPINAL FLUID IN A DOG WITH NERVOUS DISTEMPER

ABSTRACT

The purpose of this case report was to describe the haematological and biochemical analysis results of cerebrospinal fluid (CSF) in a dog diagnosed with nervous distemper. An 8-month-old female Kangal dog with complaints of involuntary contractions, mucopurulent ocular and nasal discharge, and weakness was included in the case material. The clinical examination revealed mucopurulent ocular and nasal discharge, a rectal temperature of 40.1 °C, and myoclonus in the front and back leg muscles. Canine distemper virus (CDV) antigen was detected in rapid diagnosis test kit results in ocular and nasal discharge samples, but canine influenza and canine adenovirus type 2 antigens were not. In venous blood samples taken for haematological and biochemical analysis; neutrophilic leukocytosis (14.72x109/L) was detected, while creatinine kinase-myocardial band (CK-MB) (214 U/L) and lactate dehydrogenase (LDH) (481 U/L) levels were increased. While total protein (TP) (4.84 g/dL) decreased, albumin (ALB) (2.90 g/dL) and glucose (86 mg/dL) remained within normal ranges. A 22-gauge spinal needle was used to obtain CSF from the cerebellomedullary cisternal space of an anaesthetized dog. The CSF sample contained high levels of TP (2 g/dL) and ALB (1 g/dL), as well as glucose (55 mg/dL). These values, however, were discovered to be lower than blood serum levels. A high albumin quota (AQ) ratio (34.48) was present. As a result, in cases of nervous distemper where neurological symptoms have only recently begun, the disruption of blood-brain barrier integrity caused by CDV infection causes an increase in TP and ALB levels in the CSF sample. The detection of TP and ALB levels lower than blood serum levels in CSF samples was thought to be due to the new onset of neural findings, and this situation could be used as a prognostic indicator.

Keywords: cerebrospinal fluid analysis, nervous distemper

KÖPEKLERDE ERLİŞİYOZİS VE FARKLI SAĞALTIM SEÇENEKLERİ

Prof. Dr. ALİ BİLGİLİ[1], Prof. Dr. BAŞAK HANEDAN[2]
[1]Ankara Üniversitesi Veteriner Fakültesi, Farmakoloji ve Toksikoloji Ana Bilim Dalı, Ankara, Türkiye, ORCID ID: https://orcid.org/0000-0001-6819-7952
[2]Atatürk Üniversitesi Veteriner Fakültesi, İç Hastalıkları Ana Bilim Dalı, Erzurum, Türkiye, ORCID ID: https://orcid.org/0000-0003-3873-0124

ÖZET

Erlişiyozis ve anaplazmozis kene kaynaklı enfeksiyöz hastalıklar olup, köpeklerde daha sık kedilerde daha az görülür. Hayvanlarda önemli hastalık ve ölüm oranlarına neden olduğu için *E. canis* daha fazla dikkat çekmektedir. *Ehrlichia* (*E.*) spp. ve *Anaplasma* (*A.*) spp. vektör kaynaklı patojenler *Anaplasmataceae* ailesine ait Gram negatif bakteri grubunu kapsar. *E. canis* (*Rickettsiales*; *Anaplasmataceae*) dünyada köpeklerde en yaygın şekilde görülen kene kaynaklı patojenlerden birisidir. Erlişiyoz ve anaplasmozla ilgili diğer etkenler *E. ewingii*, *E. chaffeensis*, *E. muris*, *E. ruminantium*, *A. phagocytophilum* ve *A. platys*'dir. Köpeklerde *E. canis*, *Rhipicephalus sanguineus* ve *Dermacentor variabilis*; *E. ewingii*, *Amblyomma americanum*; *E. chaffeensis*, *Amblyomma americanum* ve *Dermacentor variabilis*; *A. platys*, *Rhipicephalus sanguineus*; *A. phagocytophilum*, *Ixodes scapularis* ve *Ixodes pacificus* keneleriyle bulaştırılır. *E. canis* enfeksiyonunun seyri akut (2-4 hafta), subklinik (aylar ile yıllar) ve kronik fazlara ayrılır. Bu makale kapsamında köpeklerde önemli bir hastalık olan *Ehrlichia* ve *Anaplasma* enfeksiyonlarına neden olan etkenler sıralandı. Son yıllara ait bilimsel kaynaklar taranarak tanı ve laboratuvar bulgularına yönelik de yeni bilgiler verildi. Ayrıca sağaltımda en çok tercih edilen tetrasiklinler, rifampisin başta olmak üzere diğer ilaçlara yönelik olarak farklı sağaltım seçenekleri hakkında en yeni bilimsel kaynaklardan geniş şekilde bilgiler aktarıldı. Kene kontrolü için de ilaç uygulama konusunda kullanılan ilaçlara değinildi.
Anahtar Kelimeler: Erlişiyozis, köpek, sağaltım

EHRLICHIOSIS IN DOGS AND DIFFERENT THERAPY CHOICES

ABSTRACT

Ehrlichiosis and anaplasmosis are tick-borne infectious diseases, are appeared commonly in dogs, rare in cats. *Ehrlichia* (*E.*) *canis* draws atttention any more as causing important disease and death rates in animals. *Ehrlichia* spp. and *Anaplasma* (*A.*) spp. are vector-borne pathogens, comprise Gram negative bacteria group belonging to *Anaplasmataceae* family. *E. canis* (*Rickettsiales*; *Anaplasmataceae*) is one of the tick-borne pathogens most commonly appeared in dogs in the world. Other agents related to ehrlichiosis and anaplasmosis are *E. ewingii*, *E. chaffeensis*, *E. muris*, *E. ruminantium*, *A. phagocytophilum* and *A. platys*. In dogs, *E. canis* by *Rhipicephalus sanguineus* and *Dermacentor variabilis*; *E. ewingii* by *Amblyomma americanum*; *E. chaffeensis* by *Amblyomma americanum* and *Dermacentor variabilis*; *A. platys* by *Rhipicephalus sanguineus*; *A. phagocytophilum* by *Ixodes scapularis* and *Ixodes pacificus* ticks are transmitted. The course of *E. canis* infection is categorized to acute (2-4 weeks), subclinic (months to years) and chronic phases. In this presentation context, the agents causing *Ehrlichia* and *Anaplasma* infections, important disease in dogs were compiled. New information for diagnosis and laboratory findings was presented by searching the recent scientific sources. In addition, mainly tetracyclines, rifampicin most chose in therapy, detailed

information was presented from newest scientific sources about different therapy choices for other drugs. It was dealt with drugs used on drug application for tick control.
Keywords: Ehrlichiosis, dog, therapy

1. ETİYOLOJİ

Ehrlichia (*E.*) spp. ve *Anaplasma* (*A.*) spp. vektör kaynaklı patojenler *Anaplasmataceae* ailesine ait Gram negatif bakteri grubunu kapsar (Harrus ve Waner, 2011; Sainz ve ark., 2015). Erlişiyoz ve anaplasmozla ilgili etkenler *E. canis*, *E. ewingii*, *E. chaffeensis*, *E. muris*, *E. ruminantium*, *A. phagocytophilum* ve *A. platys*'dir (Evason, 2020).

2. EPİDEMİYOLOJİ

ABD'de 2013-2019 yıllarında *Ehrlichia* spp. antikorları %5.2 ve *Anaplasma* spp. antikorları %7.3 (Little ve ark., 2021), Meksiko'da *E. canis* %29.26 (Ojeda-Chi ve ark., 2019), Türkiye'de Trakya Bölgesi'nde *E. canis* %16 (Çetinkaya ve ark., 2016) oranlarında bildirildi.

3. BULAŞMA

Köpeklerde *E. canis*, *Rhipicephalus sanguineus* ve *Dermacentor variabilis* (Jongejan ve ark., 2016); *E. ewingii*, *Amblyomma americanum*; *A. platys*, *Rhipicephalus sanguineus* keneleriyle bulaştırılır (Evason, 2020).

4. KLİNİK BULGULAR

Genel klinik bulgular vücut sıcaklığında artma ya da düşme, bütün kan hücrelerinde azalma, halsizlik, iştahsızlık, genel lenf yumrularında büyüme, dalakta büyüme, mukozal solgunluk, kanama eğilimi ve uvea yangısıdır (Mylonakis ve ark., 2019).

5. TANI

Klinik, laboratuvar bulgular, sitoloji, floresan antikor testi, enzime bağlı immünosorbent analiz testi ve PCR testleri tanı amacıyla kullanılmaktadır.

6. SAĞALTIM

Sağaltımın amaçları klinik ve klinik patolojik bozuklukların iyileşmesi ve etkenlerin eradikasyonunu kapsar. Akut enfekte köpeklere doksisiklin 5 mg/kg dozda, ağızdan, günde 2 kez, 2-4 hafta süreyle (Shropshire ve ark., 2018) uygulanarak enfeksiyon elimine edilebilir.

KAYNAKLAR

Cetinkaya, H., Matur, E., Akyazi, I., Ekiz, E. E., Aydin, L., & Toparlak, M. (2016). Serological and molecular investigation of *Ehrlichia* spp. and *Anaplasma* spp. in ticks and blood of dogs, in the Thrace Region of Turkey. *Ticks and Tick-Borne Diseases*, *7*(5), 706-714.

Evason, M. (2020). Ehrlichiosis and Anaplasmosis. In: Weese, J. S., Evason, M. (eds). Infectious Diseases of the Dog and Cat. CRSC Press, Taylor and Francis Group,

Harrus, S., & Waner, T. (2011). Diagnosis of canine monocytotropic ehrlichiosis (*Ehrlichia canis*): an overview. *The Veterinary Journal*, *187*(3), 292-296.

Little, S., Braff, J., Place, J., Buch, J., Dewage, B. G., Knupp, A., & Beall, M. (2021). Canine infection with *Dirofilaria immitis*, *Borrelia burgdorferi*, *Anaplasma* spp., and *Ehrlichia* spp. in the United States, 2013–2019. *Parasites & Vectors*, *14*(1), 1-16.

Mylonakis, M. E., Harrus, S., & Breitschwerdt, E. B. (2019). An update on the treatment of canine monocytic ehrlichiosis (*Ehrlichia canis*). *The Veterinary Journal*, *246*, 45-53.

Ojeda-Chi, M. M., Rodriguez-Vivas, R. I., Esteve-Gasent, M. D., de León, A. A. P., Modarelli, J. J., & Villegas-Perez, S. L. (2019). *Ehrlichia canis* in dogs of Mexico: Prevalence, incidence, co–infection and factors associated. *Comparative Immunology, Microbiology and Infectious Diseases*, *67*, 101351.

Sainz, Á., Roura, X., Miró, G., Estrada-Peña, A., Kohn, B., Harrus, S., & Solano-Gallego, L. (2015). Guideline for veterinary practitioners on canine ehrlichiosis and anaplasmosis in Europe. *Parasites & Vectors*, *8*(1), 75.

Shropshire, S., Olver, C., & Lappin, M. (2018). Characteristics of hemostasis during experimental *Ehrlichia canis* infection. *Journal of Veterinary Internal Medicine*, *32*(4), 1334-1342.

KEDİLERDE PERİTONİTİS VE FARKLI SAĞALTIM SEÇENEKLERİ

Prof. Dr. ALİ BİLGİLİ[1], Prof. Dr. BAŞAK HANEDAN[2]
[1]Ankara Üniversitesi Veteriner Fakültesi, Farmakoloji ve Toksikoloji Ana Bilim Dalı, Ankara, Türkiye, ORCID ID: https://orcid.org/0000-0001-6819-7952
[2]Atatürk Üniversitesi Veteriner Fakültesi, İç Hastalıkları Ana Bilim Dalı, Erzurum, Türkiye, ORCID ID: https://orcid.org/0000-0003-3873-0124

ÖZET

Kedilerde peritonitis; primer ya da sekonder, aseptik ya da septik ve lokalize ya da generalize olarak sınıflandırılabilir. Septik peritonitis kedilerde yaygın şekilde görülen yaşamı tehdit eden önemli bir hastalıktır ve genel hayatta kalma oranı %66 olarak bildirilmektedir. Kedilerde septik peritonitis durumunda *Enterococcus, Bacillus, Pseudomonas, Tenerella, Escherichia, Streptococcus, Pasteurella, Bacteroides, Clostridium, Fusobacterium, Prevotella, Peptostreptococcus, Actinomyces, Staphylococcus, Eubacterium, Lactobacillus, Aspergillus, Flavobacterium, Porphyromonas, Corynebacterium, Mycoplasma ve Klebsiella* spp. suşlarının belirlendiği bildirildi. Başka bir çalışmada kedilerde septik peritonitis durumunda en yaygın şekilde kültürü yapılan organizmanın *Escherichia coli* olduğu, diğer izole edilen organizmaların *Pasteurella* spp., *Enterococcus faecalis*, *Bacteroides* spp., *Streptococcus* spp., *Clostridia* spp., *Proteus* spp., *Actinomyces* spp., *Staphylococcus* spp., karma anaeroblar, *Yersinia* spp., *Pseudomonas* spp. ve *Nocardia* spp. olduğu bildirildi. Bu sunum kapsamında kedilerde peritonitise neden olan başlıca etkenler sıralandı. Son yıllara ait bilimsel kaynaklar geniş şekilde irdelenerek hangi durumlarda hangi antibiyotik ya da antibiyotik kombinasyonlarının etkili olduğuna yönelik kapsamlı bilgiler verildi. Ayrıca klinisyen veteriner hekimlere pratik yönden kolaylık sağlaması bakımından, primer bakteriyel septik peritonitisli kedilerde antibakteriyel ilaç seçimleri ile kedilerde septik peritonitiste antibakteriyel sağaltım seçenekleri tablolar halinde sunuldu.
Anahtar Kelimeler: Peritonitis, antibakteriyel sağaltım, kedi.

PERITONITIS IN CATS AND DIFFERENT THERAPY CHOICES

ABSTRACT

Peritonitis can be classified as primary or secondary, aseptic or septic and localized or generalized in cats. Septic peritonitis is an important life threatening disease commonly seen in cats and general survival rate is reported as 66%. It was reported that *Enterococcus, Bacillus, Pseudomonas, Tenerella, Escherichia, Streptococcus, Pasteurella, Bacteroides, Clostridium, Fusobacterium, Prevotella, Peptostreptococcus, Actinomyces, Staphylococcus, Eubacterium, Lactobacillus, Aspergillus, Flavobacterium, Porphyromonas, Corynebacterium, Mycoplasma* and *Klebsiella* spp. strains were determined in the event of septic peritonitis of cats. In other study, in the event of septic peritonitis in cats, the most commonly isolated organism was reported to be *Escherichia coli*, other isolated organisms were reported to be *Pasteurella* spp., *Enterococcus faecalis*, *Bacteroides* spp., *Streptococcus* spp., *Clostridia* spp., *Proteus* spp., *Actinomyces* spp., *Staphylococcus* spp., mix anaerobes, *Yersinia* spp., *Pseudomonas* spp. and *Nocardia* spp. In the context of this presentation, the main agents causing peritonitis in cats were compiled. Comprehensive information was given about which antibiotic or antibiotic combinations were effective in what conditions by widely searching the recent scientific

sources. In addition, to provide convenience veterinary clinicians from a practical aspect, antibacterial drug choices in cats with primary bacterial septic peritonitis and antibacterial therapy choices in septic peritonitis in cats were presented in tables.
Keywords: Peritonitis, antibacterial therapy, cat.

1. Etiyoloji

Peritonitis primer ya da sekonder, aseptik ya da septik ve lokalize ya da generalize olarak sınıflandırılabilir.

Primer septik peritonitis karın içi enfeksiyon odağı olmadan sepsisle ilgilidir ve kedilerde seyrek olarak görülür. Primer peritonitisin en yaygın nedeni felin infeksiyöz peritonitistir (Holland, 2020).

Sekonder peritonitis septik ya da aseptik olabilir. Sekonder aseptik peritonitis mekaniksel, yabancı cisim, granülomatöz ya da sklerozan kapsüllü peritonitise kategorize edilebilir (Doom ve de Rooster, 2016).

Sekonder septik peritonitis küçük hayvanlarda peritonitisin en yaygın görülen biçimidir (Doom ve de Rooster, 2016). Peritonitisin sekonder etkeni olarak kabul edilen en yaygın neden mide-bağırsak kanalından sızmadır.

Septik peritonitis periton bölgesinin bakteri, mantar ya da mikobakterilerle bulaşmasına bağlı olarak peritonun yangısından kaynaklanır (Parsons ve ark., 2009).

2. TANI

Septik peritonitiste radyografik bulgular karın bölgesinde detay kaybını gösterir. Karın sıvısının analizinde hücre içi bakteri ve dejenere nötrofiller saptanır (Holland, 2020).

3. SAĞALTIM

Septik peritonitisin tanısı sitolojik olarak ya da periton sıvısının kültürüyle gerçekleştirilir (Anderson ve ark., 2021). Sağaltımın temeli hızlı şekilde hemodinamik stabilizasyon, enfeksiyonun kontrol altına alınması (Cioffi ve ark., 2012) ve cerrahi sağaltımdır (Costello ve ark., 2004).

Peritonitisli hastalarda izole edilen çoğu bakteri amoksisilin-klavulanik asite duyarlıdır. Yanıt vermeyen hastalarda amoksisilin-klavulanik asit, enrofloksasin ve metronidazol kombinasyonu geniş spektrum sağlar (Doom ve de Rooster, 2016).

KAYNAKLAR

Anderson, T., Beever, L., Hall, J., Moores, A., Llanos, C., Adams, R., ... & Barnes, D. (2021). Outcome following surgery to treat septic peritonitis in 95 cats in the United Kingdom. *Journal of Small Animal Practice*, *62*(9), 744-749.

Cioffi, K. M., Schmiedt, C. W., Cornell, K. K., & Radlinsky, M. G. (2012). Retrospective evaluation of vacuum-assisted peritoneal drainage for the treatment of septic peritonitis in dogs and cats: 8 cases (2003–2010). *Journal of Veterinary Emergency and Critical Care*, *22*(5), 601-609.

Costello, M. F., Drobatz, K. J., Aronson, L. R., & King, L. G. (2004). Underlying cause, pathophysiologic abnormalities, and response to treatment in cats with septic peritonitis: 51 cases (1990–2001). *Journal of the American Veterinary Medical Association*, *225*(6), 897-902.

Doom, M., & de Rooster, H. (2016). Peritonitis. In: Griffon D, Hamaide A (eds), *Complications in Small Animal Surgery*, First Edition, John Wiley and Sons, Inc., pg. 20-27.

Holland, M. (2020). Peritoneal cavity. *Feline Diagnostic Imaging*, Holland M, Hudson J (eds), First Edition, John Wiley and Sons, Inc., 529-555.

Parsons, K. J., Owen, L. J., Lee, K., Tivers, M. S., & Gregory, S. P. (2009). A retrospective study of surgically treated cases of septic peritonitis in the cat (2000–2007). *Journal of Small Animal Practice*, *50*(10), 518-524.

PİRAKLOSTROBİN'İN İNSAN MCF-7 ve MDA-MB-231 MEME KANSERİ HÜCRE HATLARI ÜZERİNDEKİ PROLİFERATİF VE METASTATİK ETKİLERİNİN ARAŞTIRILMASI

Yüksek Lisans Öğrencisi CANSU AYDIN [1], Yüksek Lisans Öğrencisi BÜŞRA ALAN [2,*], ZEKİ SERİN [3], Dr. Öğr. Üyesi, SELİN ÖZKAN KOTİLOĞLU [4], Prof. Dr., SERAP YALÇIN AZARKAN [5]

[1] KIRŞEHİR AHİ EVRAN ÜNİVERSİTESİ, Fen Bilimleri Enstitüsü, - 0000-0002-8083-7163

[2] Kırşehir Ahi Evran Üniversitesi, Fen Edebiyat Fakültesi * Maltepe Üniversitesi, Sağlık Bilimler Enstitüsü, - 0000-0002-7410-1862

[3] Kırşehir Ahi Evran Üniversitesi, Fen Edebiyat Fakültesi, - 0000-0001-6572-9706

[4] Kırşehir Ahi Evran Üniversitesi, Fen Edebiyat Fakültesi, - 0000-0002-2262-5613

[5] Kırşehir Ahi Evran Üniversitesi, Tıp Fakültesi, - 0000-0002-9584-266x

ÖZET

Meme kanseri, kadınlarda en sık görülen kötü huylu tümör olmakla beraber Dünya Sağlık Örgütü (WHO)'ne göre, her yıl 2,1 milyon kadını etkilemektedir. Meme bezlerinin sağlıklı büyümesi endokrin sistem ile sağlanmaktadır. Bu sebeple, meme kanseri risk faktörlerinin bazıları endokrin sistem ile ilişkili olduğu belirtilmiştir. Endokrin bozucu kimyasalların insan ve memeli sağlığını olumsuz etkilediği bilinmektedir. Giderek artmakta olan dünya nüfusu beraberinde kaynakların tükenmesi ve tarım alanlarında azalma ile verimsizlik sorununu beraberinde getirmiştir. Bunun önüne geçebilmek için pestisit adı verilen kimyasallar kullanılmaktadır. Piraklostrobin en yaygın kullanılan strobilurin grubu fungusitlerdendir.

Çalışmamızın amacı yaygın kullanılan bir fungisit olan piraklostrobinin östrojenik ve invaziv özellikleri açısından iki farklı meme kanseri hücre hattı üzerindeki proliferatif ve metastatik profilinin belirlenmesidir. Bu amaçla, MCF-7 ve MDA-MB-231 meme kanseri hücre hatları %10 Fetal Sığır Serumu (Fetal Bovine Serum, FBS) ve %1 Gentamisin antibiyotiği eklenmiş RPMI-1640 besiyerinde, 37°C'de ve %5 CO_2 koşulları sunan inkübatörde 75 cm^2'lik flasklarda büyütülmüştür. İki (2D) ve üç (3D) boyutlu olarak geliştirilen hücre hatlarında piraklostrobinin etkileri yara iyileşme, invazyon ve sitotoksisite deneyleri ile belirlenmiştir. Piraklostrobin maddesinin sitotoksisitesi XTT temelli sitotoksisite analiz kiti kullanılarak gerçekleştirilmiştir.

Piraklostrobin maddesinin inhibisyon konsantrasyon değerleri, MDA-MB-231 için 7 µg/ml, MCF-7 için 4.28 µg/ml olarak bulunmuştur.

Anahtar Kelimeler : Piraklastrobin, MDA-MB-231, MCF-7, meme kanseri, sitotoksisite.

INVESTIGATION OF THE PROLIFERATIVE AND METASTATIC EFFECTS OF PYRACLOSTROBIN ON HUMAN MCF-7 AND MDA-MB-231 BREAST CANCER CELL LINES

ABSTRACT

Breast cancer is the most common malignant tumor in women affecting 2.1 million women every year according to the World Health Organization. The healthy growth of the mammary glands is provided by the endocrine system. Therefore, it has been indicated that some of the breast cancer risk factors are related to the endocrine system. It is known that endocrine disrupting chemicals adversely affect human and mammalian health. The growing world population leads to depletion of resources and decrease in agricultural areas and so problems in productivity. In order to prevent this, chemicals called pesticides are used. Pyraclostrobin is the most widely used fungicide belonging to the strobilurin family.

The aim of the current study is to determine the proliferative and metastatic profile of pyraclostrobin, a widely used fungicide, on two different breast cancer cell lines in terms of estrogenic and invasive properties. Breast cancer cell lines (MCF-7 and MDA-MB-231) were grown in 75 cm^2 flasks including RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS) and 1% Gentamicin at 37°C and 5% CO_2 conditions. The effects of pyraclostrobin grown as 2D and 3D were determined by means of wound healing, invasion and cytotoxicity assays. In order to determine pyraclostrobin toxicity, XTT based analysis kit was used.

The inhibitory concentration (IC50) values of pyraclostrobin were determined as 7 µg/ml for MDA-MB-231 and 4.28 µg/ml for MCF-7.

Keywords : Pyraclostrobin, MDA-MB-231, MCF-7, breast cancer, cytotoxicity.

FLUORENE-9-BİSFENOL (BPFL)' ÜN İNSAN MCF-7 VE MDA-MB-231 MEME KANSERİ HÜCRE HATLARI ÜZERİNDEKİ SİTOTOKSİK ETKİLERİ

CANSU AYDIN [1], BÜŞRA ŞENTÜRK [2], Dr. Öğr. Üyesi, SELİN ÖZKAN KOTİLOĞLU [3], Prof. Dr., SERAP YALÇIN AZARKAN [4]

[1] KIRŞEHİR AHİ EVRAN ÜNİVERSİTESİ, Fen Bilimleri Enstitüsü,

- 0000-0002-8083-7163

[2] KIRŞEHİR AHİ EVRAN ÜNİVERSİTESİ, Fen Edebiyat Fakültesi,

- 0000-0002-3152-2544

[3] KIRŞEHİR AHİ EVRAN ÜNİVERSİTESİ, Fen Edebiyat Fakültesi,

- 0000-0002-2262-5613

[4] KIRŞEHİR AHİ EVRAN ÜNİVERSİTESİ, Tıp Fakültesi, - 0000-0002-9584-266X

ÖZET

Kanser, vücuttaki bir grup hücrenin farklılaşmasını, aşırı ve kontrolsüz çoğalması ile karakterize bir durumdur ve kadınlarda en sık görülen kanser türü meme kanseridir. Endokrin bozucu bileşikler (EDC'ler), birçok sistem hormonlar tarafından kontrol edildiğinden, endokrin sistemle ilgili üreme, nörolojik ve immünolojik süreci farklı doz seviyelerinde engelleyebilen kimyasal maddelerdir. EDC'ler, reseptörlere bağlanan doğal hormonları taklit eder ve hormonal fonksiyonları değiştirir. Bu yıkıcı etkiler, erkek ve kadın kısırlığından diyabete, obeziteye ve hormona duyarlı kanserlere kadar değişebilir. Bisfenol A (BPA) plastik üretiminde kullanılır ancak östrojenik aktiviteye sahiptir. Bu nedenle, "BPA içermeyen" plastiklerin üretimi için floren-9 bisfenol (BPFL) gibi BPA ikameleri piyasaya sürülmüştür. Bisfenol A'nın yerine geçen Floren-9- bisfenol (BPFL), endüstriyel üretim için plastiklerin kimyasal bir bileşenidir. BPFL'nin fareler üzerinde antioöstrojenik bir etki yarattığına, endometriyal atrofiyi indüklediğine ve olumsuz gebelik sonuçlarına yol açtığına dair kanıtlar vardır. Bu açıdan BPA-içermeyen ve sağlıklı olarak tanıtılan ve insanların güvenle kullanması sağlanan günlük ürünlerde bulunan BPFL' nin etkilerinin belirlenmesi büyük önem taşımaktadır.

Bu çalışmanın amacı BPA türevi olan BPFL'nin MCF-7 ve MDA-MB-231 meme kanseri hücre hatları üzerindeki sitotoksik etkilerinin araştırılmasıdır. Bu amaçla, MCF-7 ve MDA-MB-231 meme kanseri hücre hatları %10 Fetal Sığır Serumu (Fetal Bovine Serum, FBS) ve %1 Gentamisin antibiyotiği eklenmiş RPMI-1640 besiyerinde, 37°C'de ve %5 karbondioksit koşulları sunan inkübatörde büyütülmüştür. BPFL'nin sitotoksisitesi XTT temelli sitotoksisite analiz kiti kullanılarak gerçekleştirilmiştir.

BPFL maddesinin inhibisyon konsantrasyon (IC50) değerleri, MDA-MB-231 hücre hattı için 4,91 µg/ml, MCF-7 hücre hattı için 2.8 µg /ml olarak saptanmıştır.

Anahtar Kelimeler : Floren-9-bisfenol, BPFL, MDA-MB-231, MCF-7, meme kanseri, sitotoksisite.

CYTOTOXIC EFFECTS OF FLUORENE-9-BISOHENOL (BPFL) ON HUMAN MCF-7 AND MDA-MB-231 BREAST CANCER CELL LINES

ABSTRACT

Cancer is a condition characterized by the differentation, excessive and uncontrolled proliferation of a group of cells in the body, and the most common type of the cancer in women is breast cancer. Endocrine disrupting compounds (EDCs) are chemicals that can inhibit reproductive, neurological and immunological processes related to the endocrine system at different dose levels, as many systems are controlled by hormones. ECDs mimic natural hormones that bind to receptors and alter hormonal functions. These devastating effects can range from male and female infertility to diabetes, obesity and hormone-sensitive cancers. Bisphenol A (BPA) is used in the manufacture of plastics but has estrogenic activity. Thereforei BPA substitutes such as fluorene-9-bisphenol (BPFL) have been introduced fort he production of “BPA-free” plastics. BPFL, a replacement for BPA, is a chemical component of plastics for industrial production. There is evidence that BPFL exerts an anti-ostrogenic effect in mice, induces endometrial atrophy and results in adverse pregnancy outcomes. In this respect, it is of great importance to determine the effects of BPFL, which is found in daily products that are BPA-free and promoted as healthy and that people can use safely.

The aim of this study is to investigate the cytotoxic effects of BPA derivate BPFL on MCF-7 and MDA-MB-231 breast cancer cell lines. For this purpose, MCF-7 and MDA-MB-231 breast cancer cell lines were used which are grown in RPMI-1640 medium supplemented with 10% Fetal Bovine Serum (FBS) and 1% Gentamicin antibiotic at 37°C and 5% carbon dioxide conditions. The cytotoxicity of BPFL were determined by XTT based analysis kit.

Inhibitory concentration (IC50) values of BPFL were found as 4,91 µg/ml for MDA-MB-231 and 2.8 µg/ml for MCF-7.

Keywords : Fluorene-9-bisphenol, BPFL, MDA-MB-231, MCF-7, breast cancer, cytotoxicty.

EVALUATION OF PHARMACOKINETIC PROPERTIES OF *PIPER METHYSTICUM* AND *VALERINA OFFICINALIS* PLANT INGREDIENTS WITH SEDATIVE EFFECTS BY IN SILICO ANALYSIS METHOD

Asst. prof., FADİME CANBOLAT [1,*]

[1]Department of Pharmacy Services, Vocational School of Health Services, Çanakkale Onsekiz Mart University, Çanakkale, Turkey, 0000-0001-6759-7735

ABSTRACT

Piper methysticum (*Pm*) and *Valeriana officinalis* (*Vo*) are preferred and used for their sedative effects. In this study, it was aimed to determine the pharmacokinetic properties of *Pm* and *Vo* plants by in silico analysis method. Pharmacokinetic analysis of 13 molecules (*Pm* contains methysticin, dihydromethysticin, desmethoxyyangonin and *Vo* contains valtrate, valerenic acid, didrovaltrate, acevaltratum, volvalerenal A, volvalerenal B, volvalerenal C, volvalerenic acid A, volvalerenic acid B, volvalerenic acid C) were carried out by swissADME, pkCSM, and ProTox II. According to both swissADME and pkCSM results, oral absorption of all molecules was high. Methysticin, dihydromethysticin, valtrate, didrovaltrate, acevaltratum, volvalerenal A, volvalerenal C molecules appear to be a P-glycoprotein (pGP) inhibitor. Blood Brain Barrier (BBB) crossing of methysticin, dihydromethysticin, desmethoxyyangonin, valerenic acid, volvalerenal A, volvalerenal B, volvalerenal C, volvalerenic acid A, volvalerenic acid B, volvalerenic acid C molecules are comfortable. Methysticin, dihydromethysticin, valtrate, didrovaltrate, acevaltratum, volvalerenal A and volvalerenal C molecules were cytochrome P450 (CYP) 3A4 substrates. Methysticin and dihydromethysticin were CYP1A2, CYP2C19 and CYP2C9 inhibitors, and desmethoxyyangonin was CYP1A2 and CYP2C9 inhibitor. On the other hand, valtrate and didrovaltrate were CYP2D6 and CYP3A4 inhibitors, valerenic acid and volvalerenic acid A were CYP2C9 inhibitors, and acevaltratum was a CYP2D6 inhibitor. In the ProTox II, the toxic effect level of all molecules was ≥ 4.

Considering our study results, *Pm* and *Vo* plant ingredients can inhibit more than one CYP450 enzyme and pGP. Due to these properties, they have the potential to change the efficacy of drugs during the use of multiple drugs.

Keywords: *Piper methysticum, Valeriana officinalis*, In Silico, Pharmacokinetic

SEDATİF ETKİLERİ OLAN *PİPER METHYSTİCUM* VE *VALERİNA OFFİCİNALİS* BİTTİ İÇERİKLERİNİN FARMAKOKİNETİK ÖZELLİKLERİNİN İN SİLİKO ANALİZ YÖNTEMİ İLE DEĞERLENDİRİLMESİ

ÖZET

Sakinleştirici etkileri nedeniyle *Piper methysticum (Pm)* ve *Valeriana officinalis (Vo)* tercih edilir ve kullanılır. Bu çalışmada, in siliko analiz yöntemi ile *Pm* ve *Vo* bitkilerinin farmakokinetik özelliklerinin belirlenmesi amaçlanmıştır. 13 molekülün (*Pm*; metisisin, dihidrometistisin, desmetoksiyangonin'i içerir ve *Vo*; valtrat, valerenik asit, didrovaltrat, asevaltratum, volvalerenal A, volvalerenal B, volvalerenal C, volvalerenik asit A, volvalerenik

asit B, volvalerenik asit C'yi içerir) farmakokinetik analizi swissADME, pkCSM ve ProTox II ile yürütüldü. Hem swissADME hem de pkCSM sonuçlarına göre tüm moleküllerin oral absorpsiyonu yüksekti. Metisisin, dihidrometistisin, valtrat, didrovaltrat, asevaltratum, volvalerenal A, volvalerenal C molekülleri P-glikoprotein (pGP) inhibitörü gibi görünmektedir. Metisisin, dihidrometistisin, desmetoksiyangonin, valerenik asit, volvalerenal A, volvalerenal B, volvalerenal C, volvalerenik asit A, volvalerenik asit B, volvalerenik asit C moleküllerinin Kan Beyin Bariyeri (BBB) geçişi rahattır. Metisisin, dihidrometistisin, valtrat, didrovaltrat, asevaltratum, volvalerenal A ve volvalerenal C molekülleri sitokrom P450 (CYP) 3A4 substratlarıydı. Metisisin ve dihidrometistisin CYP1A2, CYP2C19 ve CYP2C9 inhibitörü, desmetoksiyangonin ise CYP1A2 ve CYP2C9 inhibitörüydü. Öte yandan valtrat ve didrovaltrat CYP2D6 ve CYP3A4 inhibitörü, valerenik asit ve volvalerenik asit A CYP2C9 inhibitörü ve asevaltratum bir CYP2D6 inhibitörüydü. ProTox II'de tüm moleküllerin toksik etki seviyesi ≥ 4 idi. Çalışma sonuçlarımız dikkate alındığında, *Pm* ve *Vo* bitki içerikleri birden fazla CYP450 enzimini ve pGP'yi inhibe edebilmektedir. Bu özelliklerinden dolayı çoklu ilaç kullanımı sırasında ilaçların etkinliğini değiştirme potansiyeline sahiptirler.
Anahtar kelimeler: *Piper methysticum, Valeriana officinalis,* in siliko, farmakokinetik

1. Introduction

Stress in our daily life brings along health problems such as sleep disorders, anxiety and depression in the future. There are many psychiatric drugs that are used to treat a variety of conditions, including sleep disorders, anxiety and depression (Karadağlı 2019). However, difficulties experienced in the supply and use of psychiatric drugs (drugs not available without a prescription, having side effects) lead people to seek for different treatments. Herbal treatments are at the forefront of these treatments. Among the reasons for preferring herbal treatments; being easily available, being economical, and considering that they are not harmful to health can be counted. *Piper methysticum (Pm)* and *Valeriana officinalis (Vo)* are among the plants that are frequently preferred and used among the public for their sedative effects (Karadağlı 2019).

Pm, is known as kava kava, the pepper of pleasure in Turkey. In Pacific culture, the plant is consumed as a daily beverage. Peeled, dried rhizomes of Pm are used. It has been reported that it inhibits cyclooxygenase and thromboxane synthesis with its bioactive substances (methysticin, dihydromethysticin, desmethoxyyangonin) (Fig.1) (Spinella 2002, Hussein 2015). *Pm* changes central gamma-aminobutyric acid (GABA) communication by blocking ion channels (Spinella 2002, Hussein 2015). *Pm* is used for restlessness, tension, sleep disorders and menopausal tension (Dinh *et al.* 2001, Thompson *et al.* 2004).

Vo, belongs to the *Valerianaceae* genus. The plant is known by names such as valerian and shepherd's cane in Turkey. The dried roots and rhizomes of *Vo* are used (Karadağlı 2019). It is used in the treatment of restlessness, nervous sleep disorders, neurological pains, dysmenorrhea (Donovan et al. 2004). Among the bioactive substances in its content are: valtrate, valerenic acid, didrovaltrate, acevaltratum, volvalerenal A, volvalerenal B, volvalerenal C, volvalerenic acid A, volvalerenic acid B, volvalerenic acid C (Fig.1) (Spinella 2002, Nandhini *et al.* 2018).

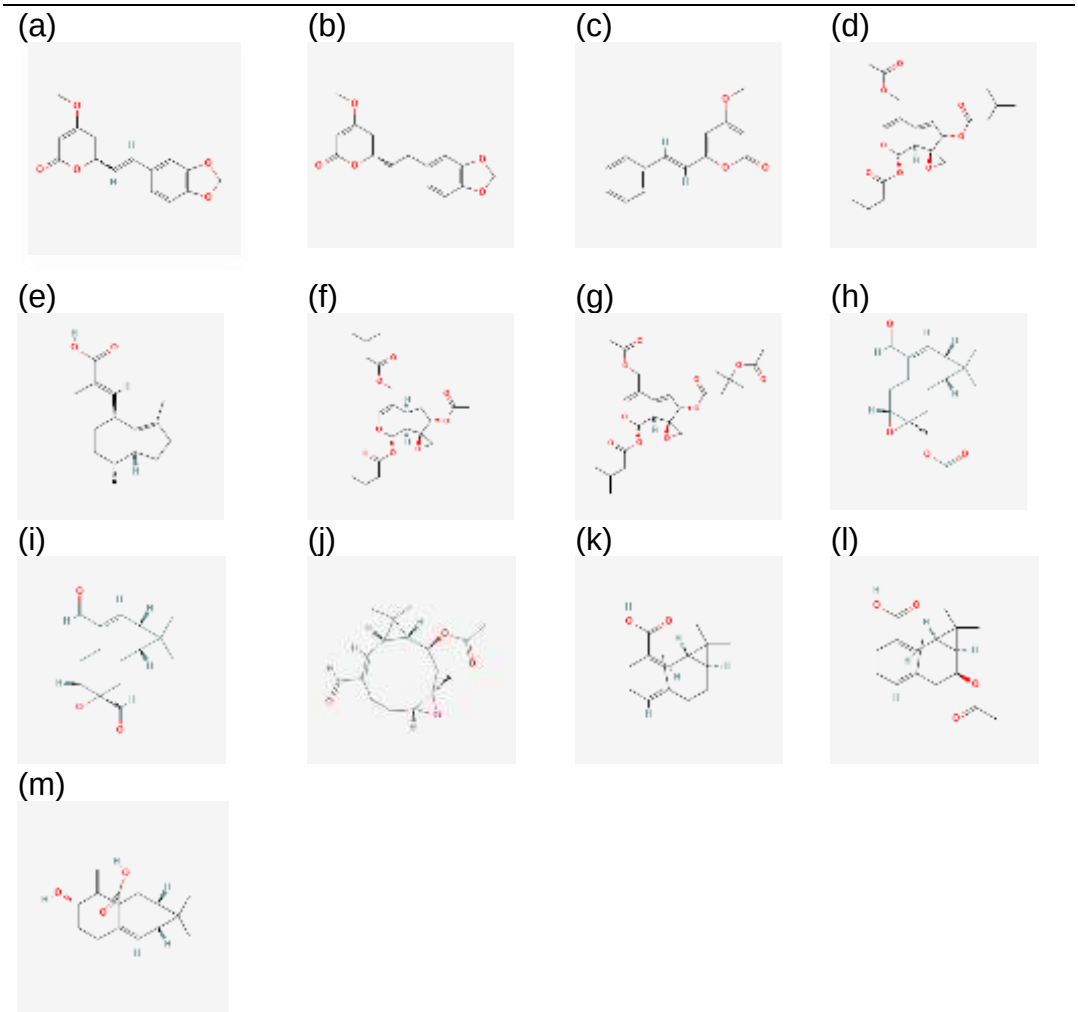

Fig.1. Major bioactive molecules of *piper methysticum (Pm)* and *valeriana officinalis (Vo)* and their chemical structures. *Methysticin (a), dihydromethysticin (b), desmethoxyyangonin (c), valtrate (d), valerenic acid (e), didrovaltrate (f), acevaltratum (g), volvalerenal A (h), volvalerenal B (i), volvalerenal C (j), volvalerenic acid A (k), volvalerenic acid B (l), volvalerenic acid C (m).*

Considering the pharmacological properties of bioactive molecules in medicinal plants, it should be noted that pharmacological interactions may also occur during the use of medicinal plants. It is necessary to stay away from wrong practices in the use of medicinal plants. When these plants are used daily, the interaction with drugs and nutrients should be taken into account (İstanbulluoğlu & Çeliker 2018). The use of medicinal plants along with psychiatric drugs used by the individual to increase the sedative effect may cause adverse reactions. Many bioactive molecules in the content of plants can interact with drugs or foods and cause toxic effects. Drugs with narrow therapeutic index and some metabolic changes may increase the possibility of interaction with the herbal product. This can cause serious health problems. Medicinal plant-drug or drug-like substance interactions are generally considered as pharmacokinetic and pharmacodynamic type interactions, which are seen as enzyme inhibition or induction (Doğan & Avcı 2018). Interaction may occur during absorption, distribution, metabolism, or excretion and can change the amount and duration of action of a drug at the site of action (Spinella *et al.* 2002, Ünverdi & Altınterim 2015). In the literature, there are in silico, in vitro and in vivo analysis methods that can determine the pharmacokinetic properties of drugs. It is seen that limited parameters can be controlled and comparative pharmacokinetic studies for more than

one molecule can not be performed adequately due to high budget and longer time requirement in pharmacokinetic studies in the literature. These reasons limit the ability of researchers to perform desirable pharmacokinetic studies. These limitations can be eliminated with in silico research models using today's technologies. The absorption, distribution, metabolism, excretion and toxicity (ADMET) parameters of molecules can be estimated using algorithms in in silico research models. In today's drug studies, in silico models are used before in vitro and in vivo analyses to eliminate the cost and time loss experienced in the drug research process. In this study, it was aimed to determine the bioactive substance interactions and pharmacokinetic properties of *Pm* and *Vo* plants, which are widely used with their sedative effects, at the pharmacokinetic level, by in silico analysis method.

2. Materials and Methods

Physicochemical and ADMET analyzes of 13 molecules (*Pm* contains methysticin, dihydromethysticin, desmethoxyyangonin and *Vo* contains valtrate, valerenic acid, didrovaltrate, acevaltratum, volvalerenal A, volvalerenal B, volvalerenal C, volvalerenic acid A, volvalerenic acid B, volvalerenic acid C) in the content of *Pm* and *Vo* plants were carried out by in silico methods. For in silico analysis, swissADME (http://www.swissadme.ch/), predicting small-molecule pharmacokinetic properties using graph-based signatures; pkCSM (http://biosig.unimelb.edu.au/pkcsm/) and prediction of toxicity of chemicals; ProTox II (https://tox-new.charite.de/protox_II/) web tools are used which can analyze the physicochemical, pharmacokinetic, drug similarity properties of molecules with fast and robust predictive models and have free access. Before in silico analysis, molecular smile structures of 13 molecules were downloaded from the "pubchem (https://pubchem.ncbi.nlm.nih.gov/)" webpage. Downloaded smile structures were uploaded to swissADME, pkCSM, ProTox II programs. The physicochemical and ADMET properties of each molecule were evaluated with the parameters in the program.

3. Results

SwissADME database analyzes data by considering 5 different evaluation (Ro5) criteria known as Lipinski, Ghose, Veber, Egan and Muegge rules in order to determine oral absorption of molecules (Lipinski *et al*.1997, Ghose *et al.* 1999, Veber *et al.* 2002). In the program, the properties of molecules with high oral absorption are determined according to the following criteria; molecular weight (MW) ≤ 500 g/mol, Hdonor ≤ 5, Hacceptor ≤ 10, MlogP ≤ 5, Polarized surface area (TPSA) <140 Å² (Lipinsky *et al.* 1997, Ghosa *et al.* 1999, Veber *et al.* 2002). The results of the physicochemical properties of 13 molecules obtained from the swissADME database are given in Table 1.

Table 1 Result of physicochemical properties of major bioactive molecules in *Pm* and *Vo* by SwissADME

Medicinal plant	Molecule	Physicochemical Properties Molecular formula	MW g/mol	TPSA Å²	H_{donor}	$H_{accept.}$	Rotb	Log $P_{O/W}$ (MLOGP)	Log S (ESOL)	Assessment of GIS, BBB and pGP subs. Status
Pm	Methysticin	$C_{15}H_{14}O_5$	274.27	53.99	0	5	3	1.47	-3.05	GIS: high BBB: Yes pGPsubs: No
	Dihydromethysticin	$C_{15}H_{16}O_5$	276.28	53.99	0	5	4	1.55	-3.12	GIS: high BBB: Yes pGPsubs: No
	Desmethoxyyangonin	$C_{14}H_{12}O_3$	228.24	39.44	0	3	3	2.06	-3.31	GIS: high BBB: Yes pGPsubs: No
Vo	Valtrate	$C_{22}H_{30}O_8$	422.47	100.66	0	8	11	1.87	-2.84	GIS: high BBB: No pGPsubs: No
	Valerenic acid	$C_{15}H_{22}O_2$	234.33	37.30	1	2	2	3.35	-3.20	GIS: high BBB: Yes pGPsubs: No
	Didrovaltrate	$C_{22}H_{32}O_8$	424.48	100.66	0	8	11	1.96	-3.18	GIS: high BBB: No pGPsubs: No
	Acevaltratum	$C_{24}H_{32}O_{10}$	480.50	126.96	0	10	13	1.48	-2.55	GIS: high BBB: No pGPsubs: No
	Volvalerenal A	$C_{17}H_{24}O_4$	292.37	55.90	0	4	4	2.11	-2.72	GIS: high BBB: Yes pGPsubs: No
	Volvalerenal B	$C_{15}H_{20}O_3$	248.32	46.67	0	3	2	1.66	-2.33	GIS: high BBB: Yes pGPsubs: No
	Volvalerenal C	$C_{17}H_{24}O_4$	292.37	55.90	0	4	3	2.11	-2.83	GIS: high BBB: Yes pGPsubs: No
	Volvalerenic acid A	$C_{15}H_{22}O_2$	234.33	37.30	1	2	1	3.35	-3.41	GIS: high BBB: Yes pGPsubs: No
	Volvalerenic acid B	$C_{17}H_{24}O_4$	292.37	63.60	1	4	3	2.83	-3.28	GIS: high BBB: Yes pGPsubs: No
	Volvalerenic acid C	$C_{15}H_{22}O_3$	250.33	57.53	2	3	1	2.47	-2.84	GIS: high BBB: Yes pGPsubs: No

Pm; piper methysticum, Vo; valeriana officinalis, MW; moleküler weight (g/mol), TPSA; topological polar surface area (Å²), H_{donor}: hydrogen donor, $H_{acceptor}$; hydrogen acceptor, Rotb; rotatable bond, GIS; gastro intestinal system, BBB; blood brain barrier, pGP subs.; p-glycoprotein substrate.

When the MW, H_{donor}, $H_{acceptor}$, TPSA, MLogP values of the molecules in Table 1 are evaluated according to the criteria determined by the program. It is seen that bioactive molecules such as methysticin, dihydromethysticin, desmethoxyyangonin in the *Pm* content are included in the Ro5 rule and their absorption in the program is high. Similarly, it is seen that bioactive molecules such as valtrate, valerenic acid, didrovaltrate, acevaltratum, volvalerenal A, volvalerenal B, volvalerenal C, volvalerenic acid A, volvalerenic acid B, volvalerenic acid C in the *Vo* content are also included in the Ro5 rule and their absorption in the program is high.

ADMET properties of methysticin, dihydromethysticin, desmethoxyyangonin, valtrate, valerenic acid, didrovaltrate, acevaltratum, volvalerenal A, volvalerenal B, volvalerenal C, volvalerenic acid A, volvalerenic acid B, volvalerenic acid C were analyzed separately in both swissADME and pkCSM data tools. Analysis results are given in Table 1 and Table 2. Table 1 presents the gastrointestinal absorption data from swissADME, Blood Brain Barrier (BBB) transition state, and P-glycoprotein (pGP) substrate status. Table 2 includes the parameters that may affect the absorption of molecules in the gastrointestinal system (GIS) using the pkCSM data tool (Pires *et al.* 2015). Solubility of molecules in water, Caco2 permeability, which is an indicator of intestinal absorption, skin permeability, and the interaction of molecules with pGP, which is one of the carrier proteins and affects absorption, is shown in Table 2.

Table 2. Result of absorption properties of of major bioactive molecules in *Pm* and *Vo* by pkCSM

Medicinal plant	Molecule	ABSORPTION						
		Water solubility Log mol/L	Caco2 permeability (log P_{APP} in 10^{-6} cm/s)	Intestinal absorption (human;% Absorbed)	Skin Permeability Log Kp	pGP subs. Yes/No	pGP I inhibitor Yes/No	pGP II inhibitor Yes/No
Pm	Methysticin	-2.60	1.35	97.5	-3.05	No	Yes	No
	Dihydromethysticin	-2.49	1.34	97.69	-3.05	No	Yes	No
	Desmethoxyyangonin	-2.90	1.53	96.85	-2.02	No	No	No
Vo	Valtrate	-4.46	0.97	98.78	-2.84	No	Yes	Yes
	Valerenic acid	-3.87	1.61	95.52	-2.70	No	No	No
	Didrovaltrate	-4.38	1.00	100	-2.88	No	Yes	Yes
	Acevaltratum	-4.57	0.97	99.14	-2.65	No	Yes	No
	Volvalerenal A	-3.36	1.33	97.50	-3.07	No	Yes	No
	Volvalerenal B	-2.99	1.29	98.05	-3.06	No	No	No
	Volvalerenal C	-3.26	1.42	98.40	-3.00	No	Yes	No
	Volvalerenic acid A	-3.03	1.60	97.02	-12.73	No	No	No
	Volvalerenic acid B	-2.95	0.89	95.58	-2.73	No	No	No
	Volvalerenic acid C	-2.63	1.29	94.68	-2.73	No	No	No

Pm; piper methysticum, Vo; valeriana officinalis, pGP subs.; p-glycoprotein substrate, pGP I inhibitor; p-glycoprotein I inhibitor, pGP II inhibitor; p-glycoprotein II inhibitor

Intestinal absorption of orally ingested molecules is performed by Caco2 permeability (Log Papp in 10^{-6} cm/s) and Intestinal absorption (human; % Absorbed) values in pkCSM web search. Since Caco2 permeability is associated with small intestinal absorption; Caco2 permeability is considered high by the pkCSM program when LogPapp > 0.90. The Caco2 permeability level provides information about the intestinal absorption of oral drugs. When the Intestinal absorption (human; % Absorbed) value is < 30% in the program output, the intestinal absorption of the molecule is evaluated as low by the pkCSM program (Pires *et al.* 2015). When Table 2 is examined, it is seen that the LogPapp level of all molecules is greater than 0.90 and the Intestinal absorption (human; % Absorbed) value is greater than 90%. According to both swissADME and pkCSM results, oral absorption of all molecules is high. SwissADME results

show that all molecules can easily pass into the brain tissue. When substrate or inhibitor status of molecules for pGP was examined, both programs showed that the molecules were not substrates for pGP. However, in the results of the pkCSM program; methysticin, dihydromethysticin, valtrate, didrovaltrate, acevaltratum, volvalerenal A, volvalerenal C molecules appear to be a pGP inhibitor. The molecules appear to be water soluble.

The results of distribution and metabolism analysis of the molecules performed via the pkCSM web tool are given in Table 3. The program includes the volume of distribution (VDss (human); Log L/kg), which affect the distribution of molecules, the level of molecules not bounded to plasma proteins (Fu), and the transition to the BBB and Central Nervous System (CNS). For metabolism analysis, evaluation is made on cytochrome P450 (CYP) enzymes, which are most effective in endogenous and exogenous substance biotransformation and are common in the hepatic and extrahepatic systems.

Table 3. Result of distribution and metabolism properties of of major bioactive molecules in *Pm* and *Vo* by pkCSM

Medicinal plant	Molecule	Distribution				Metabolism						
		VDss	Fu	BBB perm.	CNS perm.	CYP 2D6 subs.	CYP 3A4 subs.	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor
		Log L/kg		Log BB	Log PS	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
Pm	Methysticin	-0.06	0.22	-0.44	-2.38	No	Yes	Yes	Yes	Yes	No	No
	Dihydromethysticin	-0.04	0.22	-0.46	-2.50	No	Yes	Yes	Yes	Yes	No	No
	Desmethoxyyangonin	0.17	0.4	0.16	-1.61	No	No	Yes	Yes	No	No	No
Vo	Valtrate	-0.18	0.19	-1.0	-2.93	No	Yes	No	No	No	Yes	Yes
	Valerenic acid	-0.46	0.25	0.31	-2.14	No	No	No	No	Yes	No	No
	Didrovaltrate	-0.27	0.14	-1.0	-2.93	No	Yes	No	No	No	Yes	Yes
	Acevaltratum	-0.26	0.25	-1.0	-3.07	No	Yes	No	No	No	Yes	No
	Volvalerenal A	0.18	0.39	-0.19	-2.85	No	Yes	No	No	No	No	No
	Volvalerenal B	0.24	0.44	0.04	-2.95	No	No	No	No	No	No	No
	Volvalerenal C	0.17	0.39	-0.3	-2.83	No	Yes	No	No	No	No	No
	Volvalerenic acid A	-0.53	0.40	0.39	-2.73	No	No	No	No	Yes	No	No
	Volvalerenic acid B	-0.65	0.44	-0.12	-2.87	No	No	No	No	No	No	No
	Volvalerenic acid C	-0.70	0.47	-0.06	-2.89	No	No	No	No	No	No	No

Pm; piper methysticum, Vo; valeriana officinalis, VDss; human distribution volume (Log L/kg), Fu; fraction unbound (human), BBB perm.; blood brain barrier permeability (Log BB), CNS perm.; cental nervous system permeability (Log PS), CYP2D6 subs.; cytochrome P450 2D6 substrate, CYP3A4 subs.; cytochrome P450 3A4 substrate, CYP1A2 inhibitor; cytochrome P450 1A2 inhibitor, CYP2C19 inhibitor; cytochrome P450 2C19 inhibitor, CYP2C9 inhibitor; cytochrome P450 2C9 inhibitor, CYP2D6 inhibitor; cytochrome P450 2D6 inhibitor, CYP3A4 inhibitor; cytochrome P450 3A4 inhibitor.

The pkCSM web tool considers the Log VDss value when evaluating the volume of distribution of molecules. The volume of distribution of molecules with a Log VDss value of < -0.15 is considered low by the program. When Table 3 is examined, it is seen that the molecules have different distribution volumes. It is seen in the Table 3 that the Log VDss values of valtrate, valerenic acid, didrovaltrate, acevaltratum, volvalerenic acid A, volvalerenic acid B, volvalerenic acid C molecules are less than -0.15. According to the results of the analysis, it is seen that these molecules have a low volume of distribution. Crossing the BBB and passing to the CNS of molecules is evaluated with Log BB and Log PS values, respectively in the pkCSM web tool. The distribution of molecules to the brain with a Log BB value of < -1 is shown as low in the program. It is shown by the program that the CNS permeability of molecules with Log PS < -3 is low. When Table 3 is examined, Log BB value of valtrate, didrovaltrate and acevaltrate molecules is at the limit, but they can pass the BBB. It is seen in Table 3 that the BBB crossing of methysticin, dihydromethysticin, desmethoxyyangonin, valerenic acid, volvalerenal A, volvalerenal B, volvalerenal C, volvalerenic acid A, volvalerenic acid B, volvalerenic acid C molecules

are comfortable. However, CNS permeability and distribution of all molecules were found to be high when the program results were examined (Table 3). When Table 3 is examined, it is seen that methysticin, dihydromethysticin, valtrate, didrovaltrate, acevaltratum, volvalerenal A and volvalerenal C molecules are CYP3A4 substrates. In Table 3, it is seen that methysticin and dihydromethysticin molecules in the *Pm* plant content are CYP1A2, CYP2C19 and CYP2C9 enzyme inhibitors, and desmethoxyyangonin is CYP1A2 and CYP2C9 enzyme inhibitor. On the other hand, it is seen that valtrate and didrovaltrate molecules in *Vo* plant content are CYP2D6 and CYP3A4 enzyme inhibitors, valerenic acid and volvalerenic acid A molecules are CYP2C9 enzyme inhibitors, and acevaltratum molecule is a CYP2D6 enzyme inhibitor.

The excretion and toxicity analysis results of the molecules performed over the pkCSM and ProTox II web application are given in Table 4.

Table 4. Result of excretion and toxicity properties of of major bioactive molecules in *Pm* and *Vo* by pkCSM

Medicinal plant	Molecule	Excretion		Toxicity											
		CL tot. Log ml/min/kg	OCT2 subs. Yes/No	AMES Yes/No	MTD Log mg/kg/day	hERG I inhibitor Yes/No	hERG II inhibitor Yes/No	LD50 mol/kg	LOAEL Log mg/kg bw/day	Hepatotoxicity Yes/No	Skin Sensitisation Yes/No	*T.Pyriformis* toxicity Log ug/L	Minnow toxicity Log mM	Predicted LD50 (mg/kg)	Toxicity level
Pm	Methysticin	0.42	No	No	0.24	No	No	2.43	1.09	No	No	*0.89*	0.49	1130	4
	Dihydromethysticin	0.44	No	No	0.26	No	No	2.43	1.08	No	No	*0.85*	0.44	1050	4
	Desmethoxyyangonin	0.91	No	No	0.69	No	No	1.90	1.97	No	No	*0.90*	0.13	800	4
Vo	Valtrate	0.72	No	Yes	0.18	No	No	3.20	1.38	No	No	*0.31*	0.48	7500	6
	Valerenic acid	1.19	No	No	0.29	No	No	1.80	2.28	No	Yes	*0.61*	0.41	1925	4
	Didrovaltrate	0.70	No	Yes	0.18	No	No	3.22	1.43	No	No	*0.31*	0.58	7500	6
	Acevaltratum	0.62	No	Yes	0.17	No	No	3.84	1.83	No	No	*0.28*	3.89	7500	6
	Volvalerenal A	1.05	No	Yes	-0.12	No	No	2.89	1.47	No	No	*0.39*	1.3	3520	5
	Volvalerenal B	1.02	No	Yes	0.13	No	No	2.86	1.68	No	No	*0.39*	1.51	2500	5
	Volvalerenal C	1.01	No	Yes	0.04	No	No	2.92	1.39	No	No	*0.41*	1.86	3000	5
	Volvalerenic acid A	1.09	No	No	0.68	No	No	1.94	2.17	No	Yes	*0.37*	0.92	9000	6
	Volvalerenic acid B	1.09	No	No	0.82	No	No	2.12	1.87	No	No	*0.39*	1.52	5000	5
	Volvalerenic acid C	1.13	No	No	0.68	No	No	1.84	1.97	No	No	*0.27*	1.70	9000	6

Pm; piper methysticum, Vo; valeriana officinalis, CLtot; total clearance (Log ml/min/kg), OCT2 subs.; renal OCT2 substrate, AMES; AMES toxicity, MTD; maximum tolerated dose (human; Log mg/kg/day), oral rat acute toxicity- median lethal dose (LD50; mol/kg), oral rat chronic toxicity- the lowest observed adverse effect level (LOAEL; log mg/kg bw/day).

When Table 4 is examined, molecules with a Maximum Tolerable Dose (MTD; Log mg/kg/day) level less than 0.5 are seen as methysticin, dihydromethysticin, valtrate, valerenic acid, didrovaltrate, acevaltratum, volvalerenal A, volvalerenal B, volvalerenal C. None of the

molecules is an inhibitor of hERG I and hERG II. None of the molecules is hepatoxic. Valerenic acid and volvalerenic acid A can cause skin irritation. Considering the AMES mutagenicity results in Table 4; it is seen that valtrate, didrovaltrate, acevaltratum, volvalerenal A, volvalerenal B and volvalerenal C molecules may have mutagenic effects. In Minnow toxicity evaluation, LC50 (Log mM) level of desmethoxyyangonin was found to be risky according to the program criteria. In the program, LC50 < 0.5 mM is considered as high acute toxicity. In the ProTox II web application, the toxic effect levels of the molecules are shown by grading from 1 to 6 as from risky to safe. The toxicity classification was made according to the globally harmonized system of classification of labeling of chemicals (GHS), taking into account the LD50 values. There are six classes of toxicity when it comes to swallowing hazardous material: Class I (fatal if swallowed), Class II (fatal if swallowed), Class III (toxic if swallowed), Class IV (harmful if swallowed), Class V (may be harmful if swallowed), and Class VI (Non-toxic). The toxic effect level of all molecules in our study is ≥ 4.

4. Discussion

Medicinal plants, which are considered to be non-toxic due to their neutrality, may cause unexpected effects during their use when the pharmacological properties and activities of the bioactive molecules in the plant content are not known exactly. The activities of the bioactive molecules in the plant content may affect the benefit/harm ratio depending on the dose. In addition, when medicinal plants are widely consumed with different plant species, foods and/or drugs, they can cause drug-drug, drug-plant, food-plant interactions similar to polypharmacy. This may lead to a decrease in the effectiveness of the main treatment or an aggravation of the expected treatment response in individuals (Izzo & Ernst 2009).

In order to get the desired treatment response from medicinal plants, it is important to know the pharmacological properties of the bioactive molecules in the medicinal plants. Conscious and rational consumption of medicinal plants can be realized when the pharmacological properties of bioactive molecules is considered. When the ADMET properties of bioactive molecules in the content of *Pm* and *Vo*, which are frequently used in the treatment of anxiety disorders and insomnia, were examined by in silico analysis method in our study, the points to be considered about the use of these plants are given in our results.

Scientific studies to elucidate drug interaction mechanisms include drug-drug and drug-food interactions caused by pGP in pharmacokinetic interactions. In related reviews, it is reported that pGP changes the absorption and elimination process of drugs that are pGP substrates, and affects the amount of drug in plasma and brain tissue (Gül *et al*. 2016, Aypak & İnci 2017). According to the results of our analysis, it is seen in Table 1 that the absorption of methysticin, dihydromethysticin, desmethoxyyangonin, valtrate, valerenic acid, didrovaltrate, acevaltratum, volvalerenal A, volvalerenal B, volvalerenal C, volvalerenic acid A, volvalerenic acid B and volvalerenic acid C molecules is high. Table 1 shows that 13 molecules are not pGP substrates and have BBB crossing. However, in Table 2, in silico analysis results show that methysticin and dihydromethysticin in *Pm* content and valtrate, didrovaltrate, acevaltratum, volvalerenal A and volvalerenal C molecules in *Vo* content are pGP inhibitors. When the drugs that are inhibitor of pGP are used together with drugs or foods that are the substrates of pGP, they affect the pharmacokinetics and pharmacodynamics of the drugs that are pGP substrates

and may cause resistance to these drugs. By affecting the absorption and elimination process of pGP substrates, pGP inhibitor drugs can increase the plasma residence times and levels of the substrates. Concomitant use of pGP substrates with oral pGP inhibitors, can increase the therapeutic effects of pGP substrates as well as increase their side effects and toxicity. When bioactive molecules involved in *Pm* and *Vo* plant content as pGP inhibitors are used with drugs that are pGP substrates, commonly used in psychiatry (amitriptyline, citalopram, fluoxetine, fluvoxamine, paroxetine, venlafaxine, aripiprazole, risperidone, paliperidone, chlorpromazine, e.g.), and drugs that are other pGP substrates (vinkaalkoloids, taxenes, doxorubicin, daunorubicin, epirubicin, bisanthrene, etoposide, teniposite, actinomycin D, methotrexate, topotecan, saquinavir, ritonavir, nelfinavir, inapinavir, nelfinavir, colchicine, loperamide, domperidone, ondansetron, verapamil, digoxin, dexamethasone, hydrocortisone, corticosterone, triamcinolone, erythromycin, gramicidin D, valinomicin, e.g) (Aypak & İnci 2017), they may affect the pharmacokinetic properties of these drugs and cause deviations in the expected response.

Pm, which is effective in the treatment of anxiety, stress, restlessness, headache, epilepsy, insomnia in psychiatry, affects various cerebral functions in the body. It acts on GABA receptors. It increases noradrenaline and dopamine inhibition, inhibits monoamine oxidase B (MAO), binds sodium ion channel receptor (Anke & Ramzan 2004). The average recommended daily dose of *Pm* for adults is 250 mg/d (Ulbricht *et al.* 2005). It is included in the ADMET analysis data of our study that the bioactive molecules (methysticin, dihydromethysticin, desmethoxyyangonin) in the *Pm* content, which affect cerebral functions, can pass through the BBB and are easily distributed to the CNS (Table 3). As a result of the easy distribution of molecules to the CNS, it is thought that they can show their psychopharmacological activities by reaching target areas. Studies show that *Pm*, which has therapeutic efficacy, increases the effectiveness of CNS-depressants (Anke & Ramzan 2004). This effect may be the result of both pharmacokinetic and pharmacodynamic interactions.

CYP450 enzymes are involved in the biotransformation of many molecules. The combination of inhibitors or inductors of these enzymes, together with molecules that are substrates of these enzymes, can affect the plasma level of enzyme substrate molecules and change their activity in target regions. Recent studies show that bioactive molecules in *Pm* are CYP450 enzyme inhibitors (Anke & Ramzan 2004). In our study, it is seen that methysticin and dihydromethysticin molecules are both substrates and inhibitors of CYP 450 enzymes (Table 4). According to our analysis results, it is seen that methysticin and dihydromethysticin are substrates of CYP3A4 enzyme. Plasma levels of methysticin and dihydromethysticin molecules may change when inhibitor or inducer exogenous substances that affect CYP3A4 enzyme activity are used together with *Pm* plant. CYP3A4 inducers (carbamazepine, *hypericum perforatum (St. John's wort*), phenobarbital, phenytoin, rifampin) (Lynch &Neff 2007), may accelerate the biotransformation process of methysticin and dihydromethysticin molecule, causing the plasma level of the molecules to be less than expected. On the other hand, when CYP3A4 inhibitors (clarithromycin, diltiazem, erythromycin, grapefruit juice, itraconazole, ketoconazole, nefazodone, ritonavir, telithromycin, verapamil) (Lynch &Neff 2007) are used together with the *Pm* plant, it may cause the plasma level of the molecules to be higher than the expected level by slowing down the biotransformation process of methysticin and dihydromethysticin molecule. When the pharmacokinetic effect of *PM* on other drugs and foods

is examined, the fact that the bioactive molecules in the *Pm* content are CYP inhibitors can slow down the biotransformation process of the drugs and cause the plasma levels of the drugs to increase. In our study, it is seen that methysticin and dihydromethysticin molecules are CYP1A2, CYP2C19 and CYP2 C9 enzyme inhibitors, while desmethoxyyangonin molecule is an inhibitor of CYP1A2 and CYP2C9 (Table 3). When Table 3 is examined, it is seen that most of the bioactive molecules in Pm content are the inhibitors of CYP1A2, CYP2C19 and CYP2 C9 enzymes. When *Pm* plant is used with CYP1A2 enzyme substrates (amitriptyline, caffeine, diazepam, warfarin e.g), CYP2C19 enzyme substrates (amitriptyline, diazepam, imipramine, propranolol, e.g) and CYP2C9 enzyme substrates (aspirin, phenytoin, tolbutamide, warfarin), the *Pm* plant can cause an increase in the plasma level of enzyme substrates and prolong the elimination process by slowing down the biotransformation process of these enzyme substrates. Excessive consumption of *Pm* together with drugs that are CYP substrates can exacerbate the treatment response of CYP substrate drugs and cause their toxic effects. In case reports where *Pm* was used together with paroxetine, estrogens, glimeprid estrogens and pyretanide etilephrine, *Pm* has been reported to cause liver transplantation (Karadağlı 2019). In a study of Hussein in 2015, Pharmacokinetic and pharmacodynamic properties of bioactive substances in *Pm* are given. In that study, it is reported that kavain can reach its maximum plasma level within 1-2 hours, its absorption is rapid and it is excreted in the urine. It has been reported that bioactive substances in Kava inhibit CYP 450 enzymes (CYP 2C9, 2C19, 2D6, 3A4, and 1A2) in vitro (Hussein 2015, İstanbulluoğlu & Çelıker 2018). The pharmacokinetic in silico analysis results in our study are similar to the data of the study by Hussein in 2015.

In studies examining the interaction of *Pm* and alcohol, it has been observed that *Pm* and alcohol increase the toxicity of each other. It was observed in animal studies that the sleep duration of mice increased when *Pm* and alcohol are used together (Hussein 2015). In other drug interaction studies about *Pm*, it has been reported that *Pm* increases the effects of benzodiazepines and anticonvulsant drugs. However, when *Pm* is used together with levodopa, it is reported that *Pm* reduces the effect of levodopa (Izzo & Ernst 2009). In combination with paracetamol, the risk of hepatotoxicity and nephrotoxicity increases. Since concomitant use of *Pm* and opioid analgesics may cause CNS depression and increase the effect of anesthetic drugs, it is recommended to be discontinued 24 hours before the operations (İstanbulluoğlu & Çelıker 2011). It is thought that the pharmacokinetic and pharmacodynamic properties of *Pm* are effective in all these drug interactions.

In studies, lethal dose 50 (LD50) level for methysticin and dihydromethysticin, which are bioactive molecules in *Pm* content, has been reported as 920-1130 mg/kg in mice (Hussein 2015). In our study, the LD50 levels determined by the in silico analysis method are similar to those in the literature. Toxicity classification was made according to the GHS, taking into account the LD50 values in our study. In our study, the toxicity level of the bioactive substances in the *Pm* content was found to be 4. It may contain molecules that can be harmful in its content when swallowed more than the recommended daily dose ($300 < LD50 \leq 2000$).

Vo, which has sedative, muscle relaxant, sleep-inducing properties, is used in cases of restlessness, nervous agitation, lack of concentration. It has sedative and antispasmodic properties. It is a good herb in hysteria and neurasthenia, and is good for insomnia and palpitations. It is anxiolytic, The main components in the structure of *Vo* are valerenic acid and its derivatives (Anderson *et al*.2010). Valerenic acid has been shown to stimulate the secretion

of GABA and inhibit its reuptake from the synaptic gap. It has been thought that *Vo* has an effect on CNS by increasing the effect of GABA and causes potentiation together with other CNS depressants. The recommended daily dose is 600 mg/d (Kelber *et al.* 2014). *Vo* can potentiate the effects of CNS depressants . In case of concomitant use, an increase in CNS depression can be observed due to the fact that the plant shows GABA activity by binding to benzodiazepine receptors. It has been reported in studies that hand tremors, dizziness and muscle fatigue occur in patients using Vo and passiflora during lorazepam treatment (Carrasco *et al.* 2009, İstanbulluoğlu & Çelıker 2018). Because of its effects similar to benzodiazepines, abrupt discontinuation after long-term treatment may lead to withdrawal syndrome and dosage reduction is recommended. There are animal studies showing that it causes an increase in drowsiness caused by barbiturates when used together. In addition, it is seen that the combined use of *Pm* and *Vo* in the treatment of stress-induced insomnia gives a better result than single use (Karadağlı 2019).

In a study of Sampath in 2012, pharmacokinetic properties of *Vo* were studied in rats. It was stated that the absorption of *Vo* was high and its half-life (t1/2) was approximately 2 hours (Sampath *et al.* 2012). In our analysis results, the absorption of bioactive molecules in *Vo* content was found to be high. Our analysis results are similar to the literature. It has been reported that *Vo* is an inhibitor of CYP3A4 and CYP2D6 enzymes (Donovan *et al.* 2004, Gurley *et al.* 2005, Kelber *et al.* 2014). It was determined in our study that valtrate and didrovaltrate molecules in the content of *Vo* are CYP3A4 and CYP2D6 enzyme inhibitors, valeric acid and volvalerenic acid are CYP2C9 enzyme inhibitors, and acevaltum is a CYP2D6 enzyme inhibitor. In addition, it has been determined that valtrate, didrovaltrate, acevaltrum, volvalarenal A, volvalarenal C are CYP3A4 enzyme substrates. The bioactive substances in the *Vo* content have an autoinhibitory effect on the CYP3A4 enzyme. The analysis results obtained from our study are similar to those in the literature. Most of the psychiatric drugs are bio transformed via the CYP450 enzyme pathway. In addition, most of the psychiatric drugs have a narrow therapeutic range. The unconscious use of herbal products, that will reduce the biotransformation of drugs and slow down enzyme activity, along with these drugs may cause drug toxicity. Therefore, caution should be exercised when using *Vo* with psychiatric drugs because *Vo* contains bioactive molecules that inhibit more than one CYP enzyme.

Since CYP450 enzyme inducers were not shown by the program in our study, enzyme inducers could Not be included in our analysis results. In related articles, it has been reported that there are molecules in the content of *Vo* which cause a weak CYP3A4 and CYP2D6 enzyme induction in vitro (Kelber *et al.* 2014).

There are conflicting results in in vitro analysis studies with *Vo* extract. While some of the researchers showed in *in vitro* studies that valtrate and didrovaltrate have cytotoxic, mutagenic and carcinogenic activity, it was stated in other similar studies that *Vo* does not cause toxicity in vitro and in vivo (Yao *et al.* 2007). As seen in Table 4 in our study, it was determined that valtrate, didrovaltrate, acevaltrate, volvalerenal A, volvalerenal B and volvalerenal C molecules have mutagenic properties in the AMES test data. In the ProTox II web application, the toxic effect levels of the molecules are shown by classifying them from 1 to 6 from risky to safe. The toxic effect level of all molecules included in the *Vo* content in our study is $\geq$ 4. Considering our ADMET data performed with in silico analysis method, it has been determined that *Pm* and *Vo* plant content can inhibit more than one CYP450 enzyme and can inhibit pGP.

Due to these properties, it has been determined that they have the potential to change the efficacy of drugs during the use of multiple drugs.

The benefit/harm of *Pm* and *Vo* medicinal plants, which are mostly used as a mild sedative for anxiety and insomnia, were tried to be revealed in our study with in silico analysis methods. In our study, it was seen that the bioactive substances in the plant content can easily pass the BBB by meeting the Lipinski rules, thus affecting the relevant receptors and ion channels. In addition, *Pm* and *Vo* contain molecules that can cause pharmacokinetic interactions which suggests that the use of these plants in polypharmacy applications may pose a potential risk. According to the studies and our analysis results, it is revealed that the use of medicinal plants in the diet has the potential for plant-drug interaction by affecting the phenotype characteristics of the person (e.g., changes in CYP450 enzyme activity and pGp activity). It is important for human health to consider the pharmacokinetic properties and effectiveness of each medicinal product used in order to get the desired effect from the treatment.

Acknowledgment

I would like to thank Prof.Dr. Ahmet Aydın for sharing her knowledge experience.

Author Contributions

Fadime Canbolat: The author takes part in the in silico analysis, and writing of the manuscript.

Conflicts of Interest

The author declares no conflict of interest.

References

[1] Anderson, G. D., Elmer, G. W., Taibi, D. M., Vitiello, M. V., Kantor, E., Kalhorn, T. F., Howald, W.N., Barsness, S. & Landis, C. A. Pharmacokinetics of valerenic acid after single and multiple doses of valerian in older women. *Phytotherapy research*, *24*(10): 1442-1446. 2010 https://doi.org/10.1002/ptr.3151

[2] Anke, J., & Ramzan, I Pharmacokinetic and pharmacodynamic drug interactions with Kava (Piper methysticum Forst. f.). *Journal of ethnopharmacology*. *93*(2-3): 153-160. 2004. https://doi.org/10.1016/j.jep.2004.04.009

[3] Aypak, S. Ü., & İnci, A. Reason for the Ineffective Treatment: P Glycoproteins. *Bozok Tıp Dergisi*, *7*(3): 81-88. 2017.

[4] Carrasco, M. C., Vallejo, J. R., Pardo-de-Santayana, M., Peral, D., Martín, M. Á., & Altimiras, J. Interactions of Valeriana officinalis L. and Passiflora incarnata L. in a patient treated with lorazepam. *Phytotherapy Research*. *23*(12): 1795-1796. 2009. https://doi.org/10.1002/ptr.2847

[5] Dinh, L. D., Simmen, U., Bueter, K. B., Bueter, B., Lundstrom, K., & Schaffner, W. Interaction of various Piper methysticum cultivars with CNS receptors in vitro. *Planta medica*. *67*(04): 306-311. 2001.https://doi.org/10.1055/s-2001-14334

[6] Doğan, Ö., & Avcı, A. Bitkilerle tedavi ve ilaç etkileşimleri. *Turkiye Klinikleri Journal of Public Health-Special Topic*, *4*(1): 49-54. 2018.

[7] Donovan, J. L., DeVane, C. L., Chavin, K. D., Wang, J. S., Gibson, B. B., Gefroh, H. A., & Markowitz, J. S. Multiple night-time doses of valerian (*Valeriana officinalis*) had minimal effects on CYP3A4 activity and no effect on CYP2D6 activity in healthy volunteers. *Drug Metabolism and Disposition*. *32*(12):1333-1336. 2004. https://doi.org/10.1124/dmd.104.001164

[8] Ghose, A. K., Viswanadhan, V. N., & Wendoloski, J. J. A knowledge-based approach in designing combinatorial or medicinal chemistry libraries for drug discovery. 1. A qualitative and quantitative characterization of known drug databases. *Journal of combinatorial chemistry*, *1*(1): 55-68. 1999. https://doi.org/10.1021/cc9800071

[9] Gül, I. G., Eryilmaz, G., & Karamustafalioglu, K. O. P-glikoprotein ve Tedaviye Dirençteki Rolü: P-glycoprotein and its Role in Treatment Resistance. *Psikiyatride Guncel Yaklasimlar*, *8*(1): 19-31. 2016. https://doi.org/10.5455/cap.20150610111721

[10] Gurley, B. J., Gardner, S. F., Hubbard, M. A., Williams, D. K., Gentry, W. B., Khan, I. A., & Shah, A. In vivo effects of goldenseal, kava kava, black cohosh, and valerian on human cytochrome P450 1A2, 2D6, 2E1, and 3A4/5 phenotypes. *Clinical Pharmacology & Therapeutics*, *77* (5): 415-426. 2005. https://doi.org/10.1016/j.clpt.2005.01.009

[11] Hussein, A. A closer look at the risks vs. benefits of kava (*Piper methysticum*). *Journal of Student Research*, *4*(2): 69-72. 2015. https://doi.org/10.47611/jsr.v4i2.245

[12] İstanbulluoğlu, S., & Çelıker, A. İlaç-bitkisel ürün etkileşimlerinin önlenmesinde eczacının rolü. *FABAD Journal of Pharmaceutical Sciences*, *43*(3): 291-305. 2018.

[13] Izzo, A.A., & Ernst, E. Interactions between herbal medicines and prescribed drugs: an updated systematic review. *Drugs*, *69*(13): 1777-1798. https://doi.org/10.2165/11317010-000000000-00000

[14] Karadağli, S. S. 2019. Yaygın olarak kullanılan sedatif etkili tıbbi bitkiler ve ilaç etkileşimleri. *FABAD Journal of Pharmaceutical Sciences*, *44*(3): 243-253. 2009.

[15] Kelber, O., Nieber, K., & Kraft, K. 2014. Valerian: no evidence for clinically relevant interactions. *Evidence-Based Complementary and Alternative Medicine: eCAM*, 1-8. 2014.http://dx.doi.org/10.1155/2014/879396

[16] Lynch, T., & Neff, A. P. The effect of cytochrome P450 metabolism on drug response, interactions, and adverse effects. *American family physician*, *76*(3): 391-396. 2007.

[17] Lipinski, C. A., Lombardo, F., Dominy, B. W., & Feeney, P. J. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Advanced drug delivery reviews*, *23*(1-3): 3-25. https://doi.org/10.1016/j.addr.2012.09.019

[18] Nandhini, S., Narayanan, K. B., & Ilango, K. 2018. *Valeriana officinalis*: A review of its traditional uses, phytochemistry and pharmacology. *Asian J Pharm Clin Res*, *11*(1): 36-41. 1997. http://dx.doi.org/10.22159/ajpcr.2018.v11i1.22588

[19] Pires, D. E., Blundell, T. L., & Ascher, D. B. pkCSM: predicting small-molecule pharmacokinetic and toxicity properties using graph-based signatures. *Journal of medicinal chemistry*, *58*(9): 4066-4072. 2015. https://doi.org/10.1021/acs.jmedchem.5b00104

[20] Prediction of Toxicity of Chemicals-ProTox II. Charite University of Medicine Institute for Physiology Structural Bioinformatics Group, 2022. (https://tox-new.charite.de/protox_II/)

[21] pkCSM. Predicting small-molecule pharmacokinetic properties using graph-based signatures, 2022. (http://biosig.unimelb.edu.au/pkcsm/)

[22] PubChem. National Instıtutes of Health, 2022. https://pubchem.ncbi.nlm.nih.gov/

[23] Sampath, C., Haug, K., Thanei, S., Hamburger, M., Derendorf, H., Frye, R., & Butterweck, V. Pharmacokinetics of valerenic acid in rats after intravenous and oral administrations. *Planta medica*, 78 (06): 575-581. 2012. https://doi.org/10.1055/s-0031-1298301

[24] Spinella, M. The importance of pharmacological synergy in psychoactive herbal medicines. *Alternative Medicine Review*, *7*(2): 130-137. 2002.

[25] SwissADME. Swiss Institute of Bioinformatics, 2022. http://www.swissadme.ch/

[26] Thompson, R., Ruch, W., & Hasenöhrl, R. U. Enhanced cognitive performance and cheerful mood by standardized extracts of *Piper methysticum* (Kava-kava). *Human Psychopharmacology: Clinical and Experimental*, *19*(4): 243-250. 2004. https://doi.org/10.1002/hup.581

[27] Ulbricht, C., Basch, E., Boon, H., Ernst, E., Hammerness, P., Sollars, D., Tsouronis, C., Woods, J & Bent, S. Safety review of kava (*Piper methysticum*) by the Natural Standard Research Collaboration. *Expert opinion on drug safety*, *4*(4): 779-794. 2005. https://doi.org/10.1517/14740338.4.4.779

[28] Ünverdi, A., & Altınterim, B. Bitki ilaç etkileşimleri. Bilim ve Gençlik Dergisi, 3 (1): 40-45.

[29] Veber, D. F., Johnson, S. R., Cheng, H. Y., Smith, B. R., Ward, K. W., & Kopple, K. D. 2002. Molecular properties that influence the oral bioavailability of drug candidates. *Journal of medicinal chemistry*, *45*(12): 2615-2623. 2015. https://doi.org/10.1021/jm020017n

[30] Yao, M., Ritchie, H. E., & Brown-Woodman, P. D. A developmental toxicity-screening test of valerian. *Journal of ethnopharmacology*, *113*(2): 204-209. 2007. https://doi.org/10.1016/j.jep.2007.05.028

Optimization of the Process of Osmo – Convective Drying of Edible Button Mushrooms Using Response Surface Methodology (RSM)

Behrouz Mosayebi Dehkordi

Chemical Engineering Department, Islamic Azad University, Science and Research Branch, Tehran, Iran.

Abstract:

Simultaneous effects of temperature, immersion time, salt concentration, sucrose concentration, pressure and convective dryer temperature on the combined osmotic dehydration - convective drying of edible button mushrooms were investigated. Experiments were designed according to Central Composite Design with six factors each at five different levels. Response Surface Methodology (RSM) was used to determine the optimum processing conditions that yield maximum water loss and rehydration ratio and minimum solid gain and shrinkage in osmotic-convective drying of edible button mushrooms. Applying surfaces profiler and contour plots optimum operation conditions were found to be temperature of 39 °C, immersion time of 164 min, salt concentration of 14%, sucrose concentration of 53%, pressure of 600 mbar and drying temperature of 40 °C. At these optimum conditions, water loss, solid gain, rehydration ratio and shrinkage were found to be 63.38 (g/100 g initial sample), 3.17 (g/100 g initial sample), 2.26 and 7.15%, respectively.

Keywords: Dehydration, Mushroom, Optimization, Osmotic, Response Surface Methodology

The Effect of Hylocereus polyrhizus and Hylocereus undatus on Physicochemical, Proteolysis, and Antioxidant Activity in Yogurt

Zainoldin, K.H., Baba, A.S.

Zainoldin, K.H. is with Institute of Biological Sciences, Faculty of Sciences, University of Malaya, 50603 Kuala Lumpur, Malaysia
Institute of Biological Sciences, Faculty of Sciences, University of Malaya, Malaysia

Abstract:

Yogurt is a coagulated milk product obtained from the lactic acid fermentation by the action of Lactobacillus bulgaricus and Streptococcus thermophilus. The additions of fruits into milk may enhance the taste and the therapeutical values of milk products. However fruits also may change the fermentation behaviour. In this present study, the changes in physicochemical, the peptide concentration, total phenolics content and the antioxidant potential of yogurt upon the addition of Hylocereus polyrhizus and Hylocereus undatus (white and red dragon fruit) were investigated. Fruits enriched yogurt (10%, 20%, 30% w/w) were prepared and the pH, TTA, syneresis measurement, peptide concentration, total phenolics content and DPPH antioxidant inhibition percentage were determined. Milk fermentation rate was enhanced in red dragon fruit yogurt for all doses (-0.3606 - -0.4126 pH/h) while only white dragon fruit yogurt with 20% and 30% (w/w) composition showed increment in fermentation rate (-0.3471 - -0.3609 pH/h) compared to plain yogurt (-0.3369pH/h). All dragon fruit enriched yogurts generally showed lower pH readings (pH 3.95 - 4.03) compared to plain yogurt (pH 4.05). Both fruit yogurts showed a higher lactic acid percentage (1.14-1.23%) compared to plain yogurt (1.08%). Significantly higher syneresis percentage (57.19 - 70.32%) compared to plain yogurt (52.93%) were seen in all fruit enriched yogurts. The antioxidant activity of plain yogurt (19.16%) was enhanced by the presence of white and red dragon fruit (24.97- 45.74%). All fruit enriched yogurt showed an increment in total phenolic content (36.44 - 64.43mg/ml) compared to plain yogurt (20.25mg/ml). However, the addition of white and red dragon fruit did not enhance the proteolysis of milk during fermentation. Therefore, it could be concluded that the addition of white and red dragon fruit into yogurt enhanced the milk fermentation rate, lactic acid content, syneresis percentage, antioxidant activity, and total phenolics content in yogurt.

Keywords: Antioxidant activity, Hylocereus polyrhizus, Hylocereus undatus, yogurt

Comparative Analysis of Total Phenolic Content in Sea Buckthorn Wine and Other Selected Fruit Wines

Bharti Negi, Gargi Dey

Biotechnology and Bioinformatics,Jaypee University of Information Technology, Waknaghat, HP,INDIA.
Dept of Biotechnology and Bioinformatics,Jaypee University of Information Technology, Waknaghat, HP,INDIA.

Abstract:

This is the first report from India on a beverage resulting from alcoholic fermentation of the juice of sea buckthorn (Hippophae rhamnoides L) using lab isolated yeast strain. The health promoting potential of the product was evaluated based on its total phenolic content. The most important finding was that under the present fermentation condition, the total phenolic content of the wine product was 689 mg GAE/L. Investigation of influence of bottle ageing on the sea buckthorn wine showed a slight decrease in the phenolic content (534 m mg GAE/L). This study also includes the comparative analysis of the phenolic content of wines from other selected fruit juices like grape, apple and black currant. KeywordsAlcoholic fermentation, Hippophae, Total phenolic content, Wine

Keywords: Alcoholic fermentation, Hippophae, Total phenolic content, Wine

Flow Properties of Commercial Infant Formula Powders

Maja Benkovic, Ingrid Bauman

Department of Process Engineering, Faculty of Food Technology and Biotechnology, University of Zagreb, Croatia

Abstract:

The objective of this work was to investigate flow properties of powdered infant formula samples. Samples were purchased at a local pharmacy and differed in composition. Lactose free infant formula, gluten free infant formula and infant formulas containing dietary fibers and probiotics were tested and compared with a regular infant formula sample which did not contain any of these supplements. Particle size and bulk density were determined and their influence on flow properties was discussed. There were no significant differences in bulk densities of the samples, therefore the connection between flow properties and bulk density could not be determined. Lactose free infant formula showed flow properties different to standard supplement-free sample. Gluten free infant formula with addition of probiotic microorganisms and dietary fiber had the narrowest particle size distribution range and exhibited the best flow properties. All the other samples exhibited the same tendency of decreasing compaction coefficient with increasing flow speed, which means they all become freer flowing with higher flow speeds.

Keywords: flow properties, infant formula, powderedmaterial

Effects of Some Natural Antioxidants Mixtures on Margarine Stability

Maryam Azizkhani, Parvin Zandi

National Nutrition and Food Technology Research Institute, Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University, M.C. , Tehran, Iran

Abstract:

Application of synthetic antioxidants such as tertbutylhydroquinon (TBHQ), in spite of their efficiency, is questioned because of their possible carcinogenic effect. The purpose of this study was application of mixtures of natural antioxidants that provide the best oxidative stability for margarine. Antioxidant treatments included 10 various mixtures (F1- F10) containing 100-500ppm tocopherol mixture (Toc), 100-200ppm ascorbyl palmitate (AP), 100- 200ppm rosemary extract (Ros) and 1000ppm lecithin(Lec) along with a control or F0 (with no antioxidant) and F11 with 120ppm TBHQ. The effect of antioxidant mixtures on the stability of margarine samples during oven test (60°C), rancimat test at 110°C and storage at 4°C was evaluated. Final ranking of natural antioxidant mixtures was as follows: F2,F10>F5,F9>F8>F1,F3,F4>F6, F7. Considering the results of this research and ranking criteria, F2(200ppmAp + 200ppmRos) and F10(200ppmRos + 200ppmToc +1000ppmLec) were recommended as substitutes for TBHQ to maintain the quality and increase the shelf-life of margarine.

Keywords: Margarine, Natural antioxidant, Oxidative stability, Shelf-life.

Fermentative Production of Dextran using Food Industry Wastes

Marzieh Moosavi-Nasab, Mohsen Gavahian, Ali R. Yousefi, Hamed Askari

Department of Food Science and Technology, College of Agriculture, Shiraz University, Shiraz, Fars Iran

Abstract:

Dextran is a D-glucose polymer which is produced by Leuconostoc mesenteroides grown in a sucrose-rich media. The organism was obtained from the Persian Type Culture Collection (PTCC) and was transferred in MRS broth medium at 30°C and pH 6.8 for 24 h. After preparation of inoculums, organisms were inoculated into five liquid fermentation media containing either molasses or cheese whey or different combinations of cheese whey and molasses. After certain fermentation period, the produced dextran was separated and dried. Dextran yield was calculated and significant differences in different media were observed. Furthermore, FT-IR analysis was performed and the results showed that there were no significant differences in the produced dextran structures.

Keywords: Dextran, Leuconostoc mesenteroides, Molasses, Whey

Sous Vide Packaging Technology Application for Salad with Meat in Mayonnaise Shelf Life Extension

Vita Levkane, Sandra Muizniece-Brasava, Lija Dukalska

Faculty of Food Technology, Latvia University of Agriculture, Jelgava, Latvia

Abstract:

Experiments have been carried out at the Latvia University of Agriculture Department of Food Technology. The aim of this work was to assess the effect of sous vide packaging during the storage time of salad with meat in mayonnaise at different storage temperature. Samples were evaluated at 0, 1, 3, 7, 10, 15, 18, 25, 29, 42, and 52 storage days at the storage temperature of +4±0.5 ºC and +10±0.5 ºC. Experimentally the quality of the salad with meat in mayonnaise was characterized by measuring colour, pH and microbiological properties. The sous vide packaging was effective in protecting the product from physical, chemical, and microbial quality degradation. The sous vide packaging significantly reduces microbial growth at storage temperature of +4±0.5 ºC and +10±0.5 ºC. Moreover, it is possible to extend the product shelf life to 52 days even when stored at +10±0.5 ºC.

Keywords: salad with meat in mayonnaise, shelf life, sous videpackaging.

Tuberculin, Tetanus Immunoglobulin and DPT Vaccine as an Avian in vivo T-Lymphocyte Mitogens

Ibrahim Mohammed Saeed Shnawa

University of Babylon, Iraq

Abstract:

The avian phytohaemagglutinin skin test is being proved as an in vivo system for the evaluation an avian in vivo T cell mitogenicity. The test system was one week old Gallus domesticus broiler Chickens. Five replicates were done for each of the whole, 1:10 dilutions of each of 0.05 IU tuberculin, tetanus immunoglobulin and DPT vaccine as test materials. The evaluation parameters were the skin indurations and lymphoblast percentages in bone marrow lymphocytes. Tuberculin indurations were 2.06 and 1.26mm for 0.05 IU respectively while lymphoblast percent were 0.234 and 0.1 accordingly. The skin indurations of 135mg/ml and 1.35mg/ml tetanus immunoglobulin were 4.86 and 3.96mm while lymphoblast percentages were 0.3 and 0.14 respectively. The whole DPT and 1:10 concentration were with 4.5 and 3.2mm while their lymphoblast percentages were 0.28 and 0.12 accordingly. Thus the mitogenicity of the test materials was of dependant type.

Keywords: DPT, Mitogenicity, Tetenus, immunoglobulin, Tubercular.

Embryo Transfer as an Assisted Reproductive Technology in Farm Animals

Diah Tri Widayati

Gadjah Mada University, Yogyakarta, Indonesia,

Abstract:

Various assisted reproductive techniques have been developed and refined to obtain a large number of offspring from genetically superior animals or obtain offspring from infertile (or subfertile) animals. The embryo transfer is one assisted reproductive technique developed well, aimed at increased productivity of selected females, disease control, importation and exportation of livestock, rapid screening of AI sires for genetically recessive characteristics, treatment or circumvention of certain types of infertility. Embryo transfer also is a useful research tool for evaluating fetal and maternal interactions. This technique has been applied to nearly every species of domestic animal and many species of wildlife and exotic animals, including humans and non-human primates. The successful of embryo transfers have been limited to within-animal, homologous replacement of the embryos. There are several examples of interspecific and intergeneric embryo transfers in which embryos implanted but did not develop to term: sheep and goat, mouse and rat. An immunological rejections and placental incompatibility between the embryo and the surrogate mother appear to restrict interspecific embryo transfer/interspecific pregnancy. Recently, preimplantation embryo manipulation procedures have been applied, such as technique of inner cell mass transfer. This technique will possible to overcome the reproductive barrier interspecific embryo transfer/interspecific pregnancy, if there is a protective mechanism which prevents recognition of the foreign fetus by the mother of the other species

Keywords: Embryo Transfer, Assisted Reproductive Techology, Intraspesific-Interspesific Pregnancy, Inner cell mass.

Comparative Evaluation Of The Biopharmaceutical And Chemical Equivalence Of The Some Commercial Brands Of Paracetamol Tablets

Raniah Al-Shalabi, Omaima Al- Gohary, Samar Afify, Eram Eltahir

King Saud University, KSA- Saudi Arabia

Abstract:

Acetaminophen (Paracetamol) tablets are popular OTC products among patients as analgesics and antipyretics. Paracetamol is marketed by a lot of suppliers around the world. The aim of the present investigation was to compare between many types of paracetamol tablets obtained from different suppliers (six brands produced by different pharmaceutical companies in middle east countries, and Panadol® manufactured in Ireland), by different quality control tests according to USP pharmacopeia.Using Non official tests-hardness and friability; official tests-disintegration, dissolution, and drug content. Additionally, evaluate the influence of temperatures 4°C, 25°C and 40°C at 75% relative humidity on the stability of the same brands in their original packaging has been conducted for two months. The results revealed that all paracetamol tablet brands complied with the official USP specifications. In conclusion, paracetamol tablets preferred to be stored at 25°C. All the tested brands being biopharmaceutically and chemically equivalent.

Keywords: Non official tests-hardness and friability, official tests –disintegration, dissolution, and drug content.

Salbutamol Sulphate-Ethylcellulose Tabletted Microcapsules: Pharmacokinetic Study using Convolution Approach

Ghulam Murtaza, Kalsoom Farzana

Department of Pharmaceutical Sciences, COMSATS Institute of Information Technology, Abbottabad 22060, Pakistan

Abstract:

The aim of this article is to narrate the utility of novel simulation approach i.e. convolution method to predict blood concentration of drug utilizing dissolution data of salbutamol sulphate microparticulate formulations with different release patterns (1:1, 1:2 and 1:3, drug:polymer). Dissolution apparatus II USP 2007 and 900 ml double distilled water stirrd at 50 rpm was employed for dissolution analysis. From dissolution data, blood drug concentration was determined, and in return predicted blood drug concentration data was used to calculate the pharmacokinetic parameters i.e. Cmax, Tmax, and AUC. Convolution is a good biwaiver technique; however its better utility needs it application in the conditions where biorelevant dissolution media are used.

Keywords: Convolution, Dissolution, Pharmacokinetics, Salbutamol sulphate