Phytochemical and pharmacological analysis of certain plants applied in the Iranian and European folk medicine

Summary of PhD. Thesis

Javad Mottaghipisheh

Department of Pharmacognosy

Szeged

2020

University of Szeged

Doctoral School of Pharmaceutical Sciences

Pharmacognosy Ph.D. programme

Programme director: prof. dr. Judit Hohmann

Department of Pharmacognosy

Supervisor: Dr. Dezső Csupor

Javad Mottaghipisheh

Phytochemical and pharmacological analysis of certain plants applied in the Iranian and European folk medicine

Summary of Ph.D. Thesis

Defence Board:

Chair: prof. dr. Judit Hohmann

Members: dr. Attila Hunyadi,

dr. Gábor Janicsák

Assessment Board:

Chair: prof. dr. Zsolt Szakonyi, DSc

Opponents: dr. Gábor Janicsák, PhD

dr. Sándor Gonda, PhD

Members: dr. Györgyi Horváth, PhD

dr. Tamás Sovány, PhD

1. INTRODUCTION

Although medicinal plants belong to the most ancient tools of medicine, with several species having confirmed use for millennia, the first scientific data on their active constituents and mechanisms of action are not much older than 200 years. The discovery of secondary plant metabolites started in the 19th century, whereas the majority of pharmacological data was achieved in the 20th century. Compared to the huge number of plant taxa used in traditional medicine worldwide, the number of plants with confirmed efficacy, safety, elucidated mechanism of action and active constituents is infinitesimal. Plants of the European folk medicine have been studied relatively thoroughly, however, in case of several herbal drugs fundamental phytochemical and pharmacological data are missing.

The aim of the present work was to provide phytochemical and pharmacological data on some medicinal plants to support their rational use. The use of flowers of Roman chamomile (*Chamaemelum nobile*) for the symptomatic treatment of mild spasmodic gastrointestinal complaints including bloating has been acknowledged by the European Medicines Agency recommended the extract. This indication is based on the long-standing use of this plant for the listed purposes in folk medicine, however, no experimental data are available on its spasmolytic activity. Our goal was to experimentally analyse the spasmolytic effect of the plant, its essential oil and to determine the active components responsible for this effect. In case of *Matricaria chamomilla,* several metabolites responsible for the diverse biological activities have been identified, however, the systematic data on their amounts in different geographical regions are missing. Our goal was to study the phytochemical variation of samples collected in Iran, in my homeland.

In Iran, folk medicine is still a living tradition. Iranian flora is very diverse, comprising more than 8,000 vascular plant taxa, 2,597 of which are endemic or subendemic species. Several species are used for therapeutic purposes without any scientific data on their active constituents. As part of my work, we examined the secondary metabolites of two native, previously slightly studied Iranian plants, *Ducrosia anethifolia* and *Eremurus persicus.* From the six species of the *Ducrosia* genus, *D. anethifolia* is the most widely used in Iran. In folk medicine this plant is used in case of insomnia and anxiety, irregularities of menstruation, and for its carminative effect. Since based on chemotaxonomic considerations we assumed that the latter species contains furocoumarins, our goal was to study the pharmacological effects of these compounds. *E. persicus* is one of the 50 species of the genus, applied in Iranian folk medicine to treat skin diseases, as antidiabetic, and to treat gastrointestinal disorders and rheumatism.

Crocus sativus is the most important aromatic plant of Iran, with increasing importance as an aromatic plant. The stigma of *C. sativus* (saffron) has been used for the treatment of

depression and anxiety in folk medicine. Its efficacy has been confirmed in several clinical trials as well. However, the price of the raw material is a major obstacle that prevents its widespread use as medicinal drug. Other plant parts, including tepal and stamen are considered as by-products of saffron production and are not utilized industrially. Recent studies refer to antidepressant activities of these plant parts. Although the major components of tepal and stamen have already been reported, there are no systematic data on the variations and ranges of these compounds. Such data are indispensable if saffron by-products will be considered as medicinally valuable industrial raw materials.

2. AIMS OF THE STUDY

The Iranian flora comprises a wide range of plants that have been widely applied in folk medicine. Although some of these have been previously subjected to phytochemical and pharmacological analysis, many medicinal plants are still un-investigated. The plants applied in the European folk medicine have generally been studied more in detail, however, the active components and mechanisms of action of many plants of great importance are still undiscovered. The goals of our study were to:

- study the phytochemical composition and certain bioactivities of some Iranian and European medicinal plants
- review the literature on the studied plants, especially in case of the less studied Iranian medicinal plants
- isolate and identify of secondary metabolites of *Ducrosia anethifolia* and study their antiproliferative/cytotoxic effect
- isolate and identify of secondary metabolites of *Eremurus persicus*
- study the chemo-diversity of *Crocus sativus* stamens and tepals
- study the spasmolytic activity of *Chamaemelum nobile* and discover the mechanism of activity and its active components
- study the chemo-diversity of *Matricaria chamomilla* essential oils of Iranian origin

3. MATERIALS AND METHODS

Except the flowers of *C. nobile* which derived from commercial source, the flowers of *M. chamomilla*, aerial parts of *D. anethifolia* and *E. persicus*, and by-product samples of *C. sativus* (tepal and stamen) were collected from different regions of Iran.

The ethanolic (70%) extract of *C. nobile* was subjected to VLC (vacuum liquid chromatography) to prepare different fractions of 20, 40, 60, 80 and 100% methanolic in water solvents. The major constituents of the crude extract and fractions were studied by HPLC–DAD (high performance liquid chromatography-diode array detector). The methanolic extract was chromatographed by using MPLC (medium pressure liquid chromatography), GFC (gel filtration chromatography), RP-PTLC (reverse phase preparative thin layer chromatography), HPLC, and VLC on polyamide, to isolate major flavonoid contents. The essential oil (EO) was also extracted by hydro-distillation method using Clevenger-apparatus and analysed via GC–MS (gas chromatography-mass spectroscopy). All the prepared samples with pure flavonoids were assessed for their potential in smoot muscle relaxing activity.

In a comparative study, the extracted EOs of twelve *M. chamomilla* populations were quantitatively and qualitatively analysed. The antiradical capacities of their methanolic extracts were evaluated by DPPH (2,2-diphenyl-1-picrylhydrazyl) and ORAC (oxygen radical absorbance capacity) assays. HPLC–DAD fingerprinting analysis was also performed to investigate apigenin and luteolin contents of the extracts.

Isolation of the major phytochemicals of *D. anethifolia* (chloroform extract) and *E. persicus* (chloroform and ethyl acetate extracts) was accomplished by applying multi-steps chromatography techniques including CC (open column chromatography), MPLC, GFC, CPTLC (centrifugal preparative thin layer chromatography), PTLC, RP-PTLC, HPLC, and RP-HPLC. The screening was carried out by TLC (thin layer chromatography) during whole separation procedures. The structures of the isolated compounds were determined by means of spectroscopic instruments NMR (1D, 2D) and comparison of the spectra with the literature data.

Forty *C. sativus* by-product samples (40 tepals and 40 stamens), were collected from different parts of Iran. According to the literature, 7 marker compounds were determined as the major constituents and applied as the references. Validation of the analytical method was accomplished for tepal, stamen, and stigma samples by establishing the calibration curves of standards, determining the LoD (limit of detection) and LoQ (limit of quantitation) values, assessing system suitability, accuracy, precision, repeatability, stability, and filter compatibility of the extracts. Hydro-ethanolic extracts [EtOH–H_2O (1:1)] of the by-products were prepared and subjected to the HPLC–DAD fingerprinting measurements.

4. RESULTS

4.1. CHAMAEMELUM NOBILE

According to the HPLC–DAD results, four main peaks were characterised from crude extract of *C. nobile*. The corresponding components were isolated and identified as the flavonoids apigenin, eupafolin, hispidulin, and luteolin (**Figure 1**). These compounds were used as reference standards to characterize the crude extract of *C. nobile* and fractions obtained from VLC (F20, F40, F60, F80, F100). The crude extract of *C. nobile* comprised eupafolin as the main flavonoid, followed by luteolin, hispidulin, and apigenin. The flavonoid content of the fractions increased with increasing MeOH content of the eluting solvent. The highest flavonoid levels were measured in F80 (80% MeOH), except for luteolin and apigenin, which were mainly concentrated in F100 (pure MeOH).

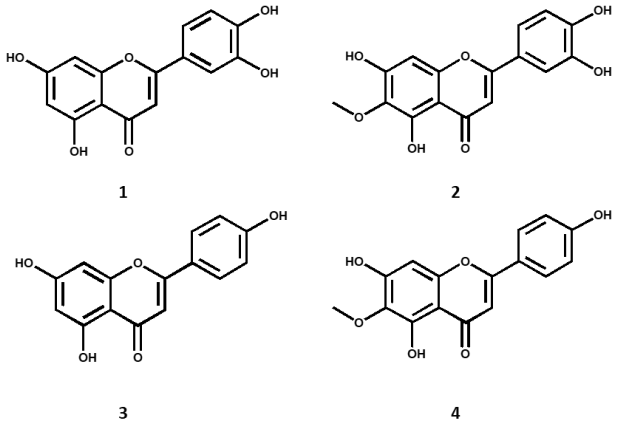

Figure 1. The chemical structures of the isolated flavonoids from *Chamaemelum nobile*; **1**: luteolin; **2**: eupafolin; **3**: apigenin; **4**: hispidulin

GC–MS results determined methallyl angelate, 3-methyl pentyl angelate, and 3-methylamylisobutyrate as the major constituents of *C. nobile* EO (19.0, 18.2, and 10.4%, respectively). The crude extract of *C. nobile* induced a transient longitudinal contraction on guinea pig ileum preparations. Both atropine (an antagonist of acetylcholine at the muscarinic receptors) and tetrodotoxin (an inhibitor of voltage-sensitive Na^+ channels; hence, of neuronal axonal conduction) inhibited the contractile effect of *C. nobile* crude extract. The functional blockade of capsaicin-sensitive neurons did not inhibit, whereas the cyclooxygenase inhibitor indomethacin moderately inhibited the contraction in response to the *C. nobile* extract. Subfractions of the crude extract also possessed contracting activity.

After transient contraction, smoot muscle relaxing activity was observed. On histamine-precontracted preparations (in the presence of atropine and tetrodotoxin), concentration-

dependent relaxation was observed in response to treatment with *C. nobile* crude extract (60–200 µg/mL). The highest tested concentration induced full relaxation. Different fractions of the *C. nobile* extract demonstrated distinct relaxant effects. F20 and F40 (60 or 200 µg/mL) produced no relaxation, whereas F60, F80 and F100 had remarkable and dose-dependent spasmolytic activity in this concentration range (up to 100%). This observation refers to the potential role of flavonoids in the relaxant effect, and experiments with four flavonoids isolated from the plant material reassured this hypothesis. The four major flavonoids of the extracts (hispidulin, luteolin, eupafolin and apigenin) had relaxant activities at 2 µM ranging between 18.2–24.2%, whereas at 20 µM between 64.5–81.9%. The EO (0.1–10 µg/mL) induced 12.8–69.7% relaxation in dose-dependent manner with no pre-contraction.

4.2. MATRICARIA CHAMOMILLA

The EO, and flavonoid contents of the various *M. chamomilla* were affected by the growth environment. The EO yields ranged from 0.78 ± 0.017% to 1.03 ± 0.003% in populations "Bagh Malek" and "Bodgold" (cultivated sample), respectively. Among seventeen identified compounds, sesquiterpene *α*-bisabolone oxide A (45.64–65.41%) was the major EO constituent in the samples except "Bodgold" and "Sarableh". The cultivated sample "Bodgold" was rich in *α*-bisabolol oxide B (21.88%) and chamazulene (19.22%).

The HPLC–DAD results indicated that the methanolic extracts of "Lali" and "Bagh Malek" contained the highest amounts of apigenin and luteolin with 1.19 ± 0.01 and 2.20 ± 0.0 mg/g, respectively. Cluster (CA) and principle component analysis (PCA) were used to classify the studied populations according to their EO compositions and apigenin and luteolin contents. In accordance with the CA, the populations "Izeh", "Darreh Shahr", "Mollasani", "Masjed Soleyman", "Murmuri", "Gotvand", "Saleh Shahr", "Lali", "Abdanan" and "Bagh Malek" were classified into the same category, while, "Bodgold" and "Sarableh" were grouped into the individual subclasses. The first group possessed *α*-bisabolone oxide A and *α*-bisabolol oxide A as the major constituents as well as apigenin and luteolin (chemotype I). The second chemotype (II), was characterized by high amounts of chamazulene and *α*-bisabolol oxide B, while the chemotype (III) was the richest in (*Z*) and (*E*)-*γ*-bisabolene.

Moreover, "Sarableh" showed the most significant antiradical capacity, with EC_{50} of 7.76 ± 0.3 µg/mL and 6.51 ± 0.63 mmol TE/g measured by DPPH and ORAC assays, respectively. However, the extracts showed lower activity compared to ascorbic acid (EC_{50} = 0.3 ± 0.02 µg/mL) in the DPPH and rutin (20.22 ± 0.63 mmol TE/g) and EGCG (11.97 ± 0.02 mmol TE/g) in the ORAC assay.

4.3. DUCROSIA ANETHIFOLIA

Repeated column chromatography (CC, MPLC, CPTLC, RP-HPLC, and PTLC) of the bioactive fractions resulted in the isolation of 13 compounds (**Figure 2**). The compounds were identified by interpretation of NMR data and comparison of ^{1}H and ^{13}C chemical shifts with those reported in literature. Nine linear furocoumarin derivatives, namely imperatorin (**5**), oxypeucedanin (**7**), heraclenol (**8**), (+)-oxypeucedanin hydrate (aviprin) (**9**), heraclenin (**10**), pabulenol (**11**), oxypeucedanin methanolate (**13**), isogospherol (**14**), (–)-oxypeucedanin hydrate (prangol) (**16**); along with vanillic aldehyde (**6**), 3-hydroxy-*α*-ionone (**12**), harmine (**15**), and 2-*C*-methyl-erythrytol (**17**) were identified (**Figure 3**). Compounds 6, 7, 9, 12, 14–17 were identified for the first time in the *Ducrosia* genus.

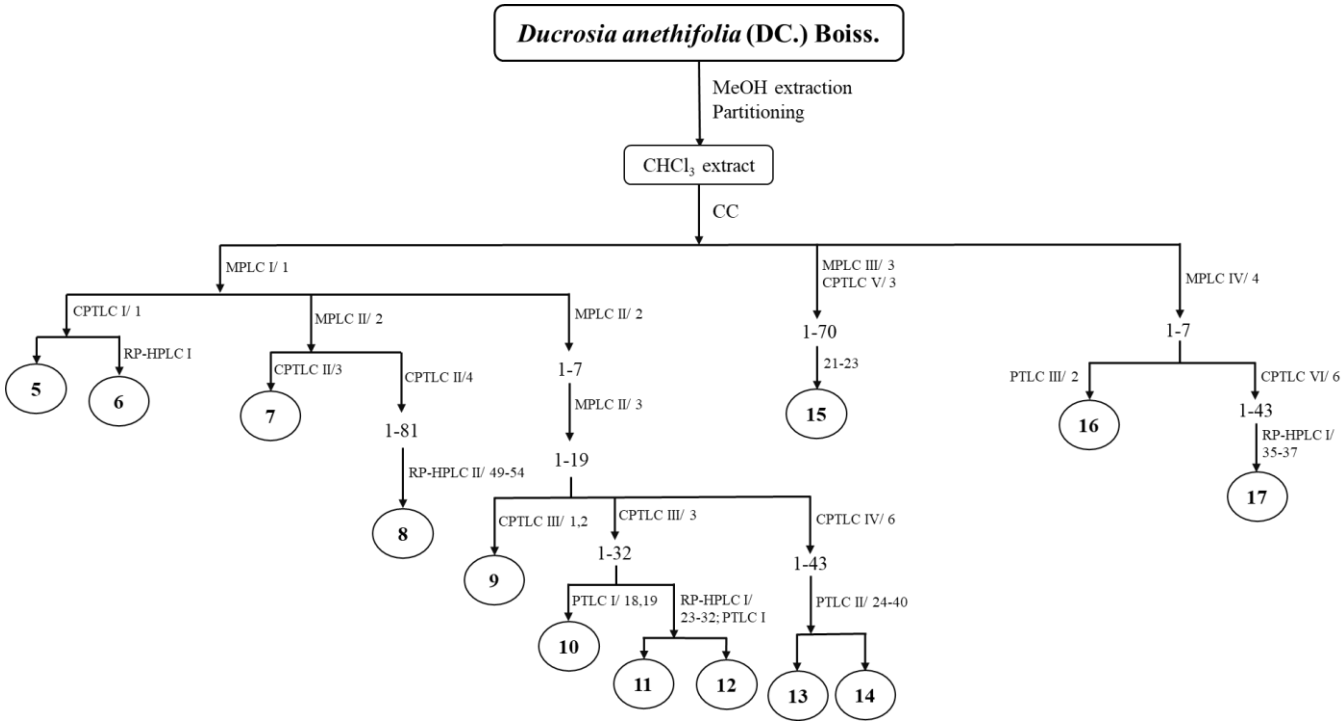

Figure 2. Isolation of pure compounds from *Ducrosia anethifolia*

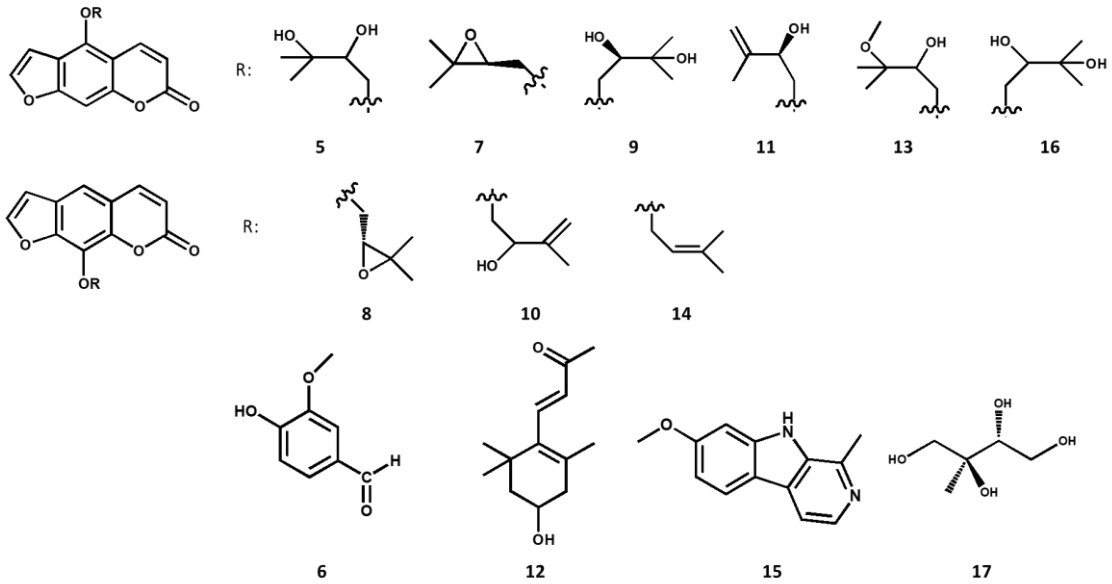

Figure 3. Secondary metabolites isolated from *D. anethifolia*

The furocoumarins isolated from *D. anethifolia* were subjected to assess cytotoxic and antiproliferative activity against cancer cell lines including sensitive (PAR) and resistant mouse T-lymphoma (MDR), and normal murine fibroblast (NIH/3T3) cells. The most potent antiproliferative compound was oxypeucedanin (**7**) on both PAR and MDR cells. Furthermore, imperatorin (**5**), pabulenol (**11**), and oxypeucedanin methanolate (**13**) were more toxic on the PAR cell line (IC_{50} between 52 and 57 mM) without any toxicity on MDR cells.

Oxypeucedanin (**7**) and heraclenin (**10**) exhibited cytotoxic activity; however, they were more potent on the PAR cell line. Oxypeucedanin (**7**), heraclenin (**10**), and oxypeucedanin methanolate (**13**) exhibited mild toxicity on fibroblasts and parental lymphoma cells. Imperatorin (**5**) had no toxic activity on fibroblasts. Regarding the efflux pump inhibiting activity of the compounds on ABCB1 overexpressing MDR mouse T-lymphoma cells, only oxypeucedanin (**7**) showed moderate ABCB1 inhibiting effect (FAR: 2.22); however, this inhibition was lower than the positive controls tariquidar (FAR: 100) and verapamil (FAR: 8.2).

Two most promising compounds oxypeucedanin (**7**) and heraclenin (**10**) in the previous assays were investigated in combination with the standard chemotherapeutic drug doxorubicin. Both showed slight synergistic effect with doxorubicin, for this reason, they might be potential adjuvants in combined chemotherapy applying standard anticancer drugs with compounds that can act synergistically.

4.4. EREMURUS PERSICUS

As shown in **Figure 4** six pure compounds were isolated by hiring successive chromatography steps *via* FC (flash chromatography), MPLC, GFC, CPTLC, PTLC and RP-PTLC. A rare glucoside aliphatic alcohol corchoionoside A (**18**), 4-amino-4-carboxychroman-2-one (**19**), a *C*-glycosyl flavone isoorientin (**20**) from ethyl acetate extract, and ziganein 5-methyl ether (**21**), and two coumarin derivatives namely auraptene (**22**), and imperatorin (**23**) from chloroform extract were isolated and identified by 1D, 2D NMR and comparison with literature. Except isoorientin (**20**) all the compounds were isolated for the first time in the *Eremurus* genus. The chemical structures of the isolated compounds are given in **Figure 5**.

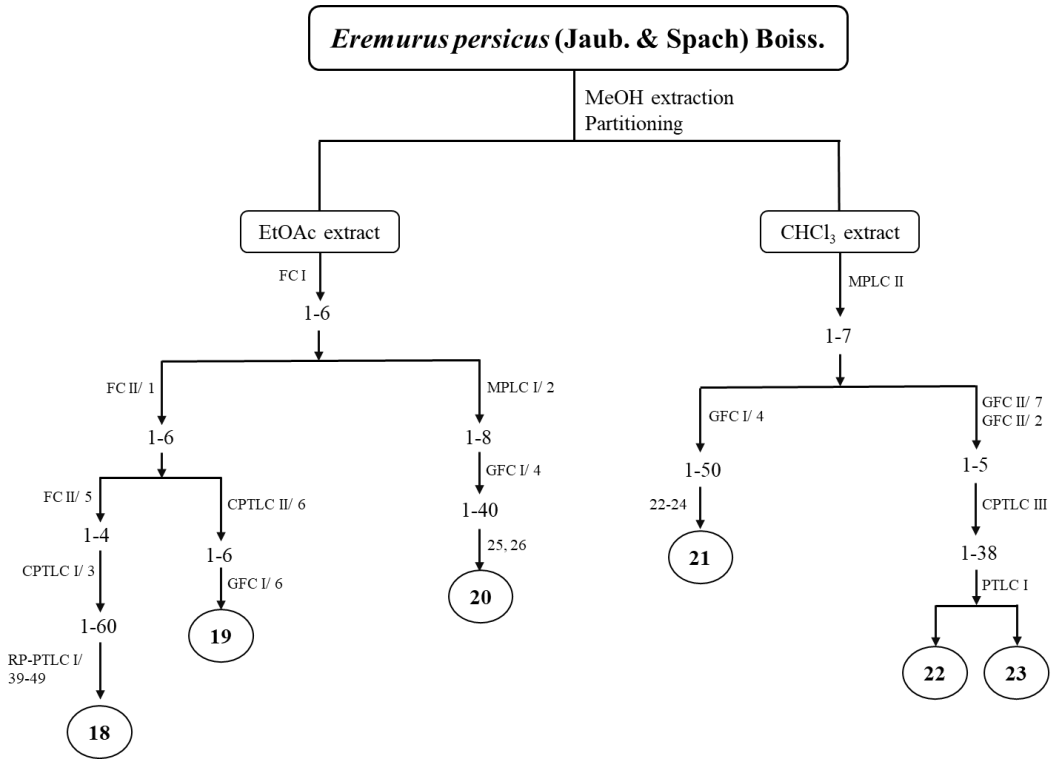

Figure 4. Isolation of the compounds from *Eremurus persicus*

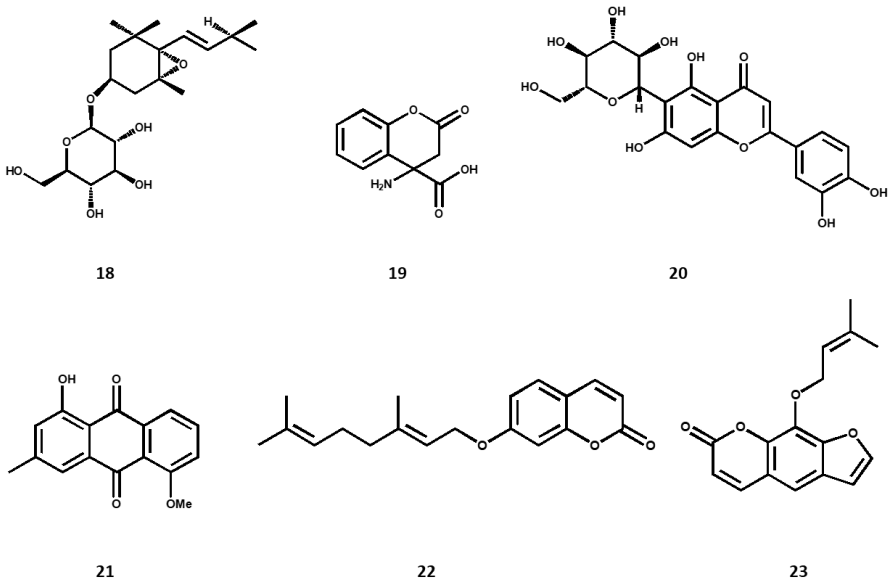

Figure 5. The chemical structures of the isolated phytochemicals of *Eremurus persicus*

4.5. CROCUS SATIVUS

Our aim was to validate and develop an analytical method that is suitable for the analysis of saffron crocus (*C. sativus*) stigma and by-products samples. Marker compounds, that were used as reference standards during our experiments were chosen based on literature data as follows: safranal (**24**), picrocrocin (**25**), crocetin (**26**), crocin (**27**), kaempferol-3-*O*-glucoside (K.G.) (**28**), quercetin-3-*O*-sophoroside (Q.S.) (**29**), and kaempferol-3-*O*-sophoroside (K.S.) (**30**). During validation, tepal samples and the mixture of the reference compounds were used. Validation was carried out for all the analytes, where possible. The validation was partial for crocin, crocetin, picrocrocin, and safranal, due to these compounds did not contain in saffron crocus tepal. The chemical structures of the marker compounds are displayed in **Figure 6**.

Forty different tepal and stamen samples were subjected to HPLC–DAD analysis to qualitatively and quantitatively analyse their selected markers. Our developed HPLC method allowed the good separation and hence the reliable analysis of these compounds in saffron crocus samples. In tepal and stamen samples only three glycosylated flavonols including Q.S., K.S., and K.G. were detected. We analysed a saffron stigma sample as well. From this sample picrocrocin, crocin, and crocetin were identified, which is in line with previous data.

The tepal samples comprised Q.S., K.S. and K.G., in the ranges of 6.20–10.82, 62.18–99.48, and 27.38–45.17 mg/g, respectively, whereas the amount of these compounds was lower in stamen (1.72–6.07, 0.89–6.62 and 1.72–7.44 mg/g, respectively). Sample 1 contained the highest content of K.S. (99.48 mg/g) as the major constituent of tepal. Moreover, the tepal sample 23 possessed the highest amount of Q.S. (10.82 mg/g), while the tepal sample 5 contained the lowest amounts of Q.S. and K.S. with 6.21 and 62.19 mg/g, respectively. In tepal

samples the K.G. content ranged between 27.74 to 45.18 mg/g in samples 40 and 1, respectively. In general, the stamen samples contained less flavonoids than tepals. The highest amount of Q.S. in stamens was observed in sample 29 with 6.08 mg/g, whilst sample 3 contained the lowest concentration (1.63 mg/g). The quantity of K.S. ranged from 6.62 to 0.93 mg/g in stamen samples 40 and 3, respectively. The quantity of the flavonoid K.G. was also variable, the highest and lowest amounts determined in sample 31 and 8 with 7.44 and 1.72 mg/g, respectively.

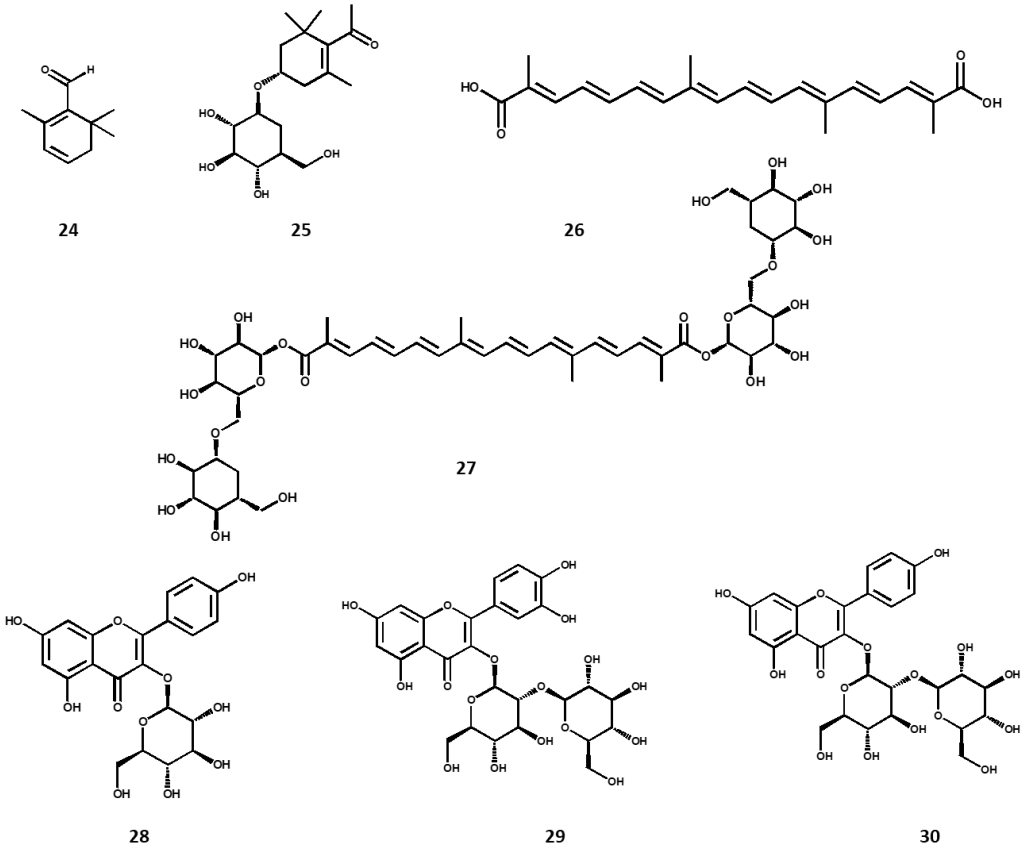

Figure 6. The chemical structures of the reference compounds of *Crocus sativus* L.; **24**: safranal; **25**: picrocrocin; **26**: crocetin; **27**: crocin; **28**: kaempferol-3-*O*-glucoside; **29**: quercetin-3-*O*-sophoroside; **30**: kaempferol-3-*O*-sophoroside

CA and PCA were applied to characterize and classify saffron crocus samples (tepal and stamen) collected from different locations in Iran according to their Q.S., K.S., and K.G. contents. In accordance with the CA analysis, the saffron crocus samples harvested from various locations were categorized in three major groups showing three distinct chemotypes based on their flavonoid contents. Chemotype I was characterized with the highest Q.S. content of in tepal samples, including the populations 2, 3, 6-12, and 39; samples belonging to chemotype II contained high quantity of K.G. in tepal samples (populations 4, 5, 13, 14, 16–18, 22, 24, 26–30, 32-34, and 37); whereas chemotype III was the richest in Q.S., K.S., and K.G. in stamen, and K.S. in tepal (populations 1, 15, 16, 19-21, 23, 25, 31, 35, 36, 38, 40).

5. SUMMARY

The work presented here was aimed at investigating the secondary metabolites of Iranian and European medicinal plants. We verified the folk medicinal use of *Chamaemelum nobile* for its antispasmodic potential. The smooth muscle relaxant effect seemed to be associated with the flavonoid content of the plant. The essential oil also has a remarkable smooth muscle relaxant effect in this setting.

Growth geographical conditions extensively affected the volatile oil compositions, flavonoid contents, and antiradical capacities of twelve *Matricaria chamomilla* populations collected from Iran. Among seventeen identified volatile components, representing more than 90% of the total oil, *α*-bisabolone oxide A was the major constituent, except the sample "Sarableh", a new chemotype, where (*E*)- and (*Z*)-*γ*-bisabolene were the predominant components.

Ducrosia anethifolia was subjected to isolate the secondary metabolites, subsequently, 13 pure compounds including 9 furocoumarins were isolated. Eight of the phytochemicals were identified for the first time in the genus. Among the furocoumarins, oxypeucedanin (**7**) and heraclenin (**10**) possessed promising antiproliferative and cytotoxic activities against two selected cancer cell lines. Six pure compounds were isolated from a scarce Iranian herb namely *Eremurus persicus*, 5 of which were characterised as the new compounds in the genus.

We developed a comprehensive validation method for HPLC-DAD fingerprinting analysis of 7 major compounds of different *Crocus sativus* plant parts. The by-products of saffron crocus production, specifically tepals can be considered as rich sources of flavonols. Kaempferol-3-*O*-sophoroside and kaempferol-3-*O*-glucoside were identified as the most dominant phytochemicals in tepal and stamen samples, respectively. Crocin, crocetin, picrocrocin, and safranal were not detected in any of the analysed samples (except stigma). The data presented here can be useful in setting quality standards for plant parts of *C. sativus* that might be used for medicinal purposes in the future.

ACKNOWLEDGMENTS

I wish to express my sincere appreciation to my supervisor, ***Assoc. Prof. Dr. Dezső Csupor***, who has the substance of a genius: he convincingly guided and encouraged me to be professional and do the right thing even when the road got tough. Without his persistent help, the goal of this project would not have been realized.

I am deeply indebted to ***Prof. Judit Hohmann*** as head of the Department of Pharmacognosy for providing me all the opportunities to perform experimental work.

My special thanks to all of my friends in the lab, whose assistance was a milestone in the completion of this project ***Dr. Tivadar Kiss***, ***Attila Horváth***, ***Dr. Zoltán Péter Zomborszki***, ***Dr. Martin Vollár***, ***Dr. Diána Kerekes***, ***Balázs Kovács***, and ***Háznagyné Dr. Erzsébet Radnai***, besides whole the staff members at the Department of Pharmacognosy for their valuable help and support, specifically ***Dr. Norbert Kúsz*** and ***Dr. Yu-Chi Tsai*** for the NMR experiments.

I am very grateful to Department of Pharmacology and Pharmacotherapy, Department of Pharmacognosy, and Department of Surgery, University of Pécs, Pécs, Hungary, and Department of Medical Microbiology and Immunobiology, Faculty of Medicine, University of Szeged, Szeged, Hungary for assessing the pharmacological activities, and Department of Horticultural Science, Faculty of Agriculture, Shahid Chamran University of Ahvaz, Ahvaz, Iran, for analysing the essential oils.

I wish to dedicate this work to my wife, Nasim who her patience that cannot be underestimated, my parents, who have always urged me, the soul of my brother, and my nephews. This thesis would not have been possible without their love, encouragement, and appreciation for higher education.

LIST OF PUBLICATIONS RELATED TO THE THESIS

1. Sándor Z[1], **Mottaghipisheh J[1]**, Veres K, Hohmann J, Bencsik T, Horváth A, Kelemen D, Papp R, Barthó L, Csupor D.
   Evidence supports tradition: the *in vitro* effects of Roman chamomile on smooth muscles.
   Frontiers in Pharmacology Ethnopharmacology 2018, 9: 323.
   IF (2017): 4.4, D1

2. **Mottaghipisheh J**, Nové M, Spengler G, Kúsz N, Hohmann J, Csupor D.
   Antiproliferative and cytotoxic activities of furocoumarins of *Ducrosia anethifolia*.
   Pharmaceutical Biology 2018, 56: 658-664.
   IF (2017): 1.91, Q1

3. Piri E, Mahmoodi Sourestani M, Khaleghi E, **Mottaghipisheh J**, Zomborszki ZP, Hohmann J, Csupor D.
   Chemo-diversity and antiradical potential of twelve *Matricaria chamomilla* L. accessions from Iran: a proof of ecological effects.
   Molecules 2019, 24, pii: E1315.
   IF (2018): 3.06, Q1

4. **Mottaghipisheh J**, Mahmoodi Sourestani M, Kiss T, Horváth A, Tóth B, Ayanmanesh M, Khamushi A, Csupor D.
   Comprehensive chemotaxonomic analysis of saffron crocus tepal and stamen samples, as raw materials with potential antidepressant activity.
   Journal of Pharmaceutical and Biomedical Analysis 2020, 184, 113183.
   IF (2018): 2.983, Q1

PRESENTATIONS RELATED TO THE THESIS:

1. **Mottaghipisheh J**, Nové M, Spengler G, Kúsz N, Hohmann J, Csupor D.
   Phytochemical and pharmacological analysis of two Iranian plants, *Ducrosia anethifolia* and *Eremurus persicus.*
   25th International Symposium on Analytical and Environmental Problems, Szeged, Hungary, 2019, oral presentation.

[1] Both authors contributed equally to this work

2. **Mottaghipisheh J**, Kúsz N, Hohmann J, Tsai Y, Csupor D.

Isolation and structural elucidation of secondary metabolites from *Eremurus persicus.*

Trends in Natural Product Research - PSE Young Scientists' Meeting on Biochemistry, Molecular Aspects and Pharmacology of Bioactive Natural Products, Budapest, 2019, poster presentation.

3. **Mottaghipisheh J**, Márta N, Spengler G, Kúsz N, Hohmann J, Csupor D.

Antiproliferative and cytotoxic activities of furocoumarins of *Ducrosia anethifolia.*

Fiatal Gyógynövénykutatók Fóruma, Szeged, Hungary, 2018, oral presentation.

4. **Mottaghipisheh J**, Spengler G, Márta N, Kúsz N, Hohmann J, Csupor D.

Antiproliferative and cytotoxic activities of furocoumarins of *Ducrosia anethifolia.*

Advances in Phytochemical Analysis (Trends in Natural Products Research), PSE young scientists' meeting, Liverpool, UK, 2018, poster presentation.

LIST OF OTHER PUBLICATIONS

1. Mahmoodi Sourestani M, Piri E, **Mottaghipisheh J**, Vitalini S, Iriti M.

Monthly changes in contents and compositions of oil of *Callistemon citrinus*: A comparison study.

Natural Product Research 2020, [Epub ahead of print].

(IF: 1.99, Q2)

2. Boveiri Dehsheikh A, Mahmoodi Sourestani M, Boveiri Dehsheikh P, **Mottaghipisheh J**, Vitalini S, Iriti M.

Monoterpenes: Essential oil components with valuable features.

Mini-Reviews in Medicinal Chemistry 2020, 20(1), [Epub ahead of print].

(IF: 2.84, Q2)

3. Bagherifar S, Mahmoodi Sourestani M, Zolfaghari M, **Mottaghipisheh J**, Zomborszki ZP, Csupor D.

Variation of chemical constituents and antiradical capacity of nine *Ferulago angulata* (Schltdl.) Boiss. populations from Iran.

Chemistry & Biodiversity 2019, 16(10), e1900302.

(IF: 1.44, Q2)

4. Bagherifar S, Mahmoodi Sourestani M, Zolfaghari M, **Mottaghipisheh J**, Zomborszki ZP, Csupor D.

Chemodiversity of volatile oil contents of various parts of 10 Iranian *Prangos ferulacea* accessions, with analysis of antiradical potential.

Natural Product Communications 2019, 14(5).

(IF: 0.55, Q2)

5. Boveiri Dehsheikh A, Mahmoodi Sourestani M, Boveiri Dehsheikh P, Vitalini S, Iriti M, **Mottaghipisheh J**.

A comparative study of essential oil constituents and phenolic compounds of Arabian lilac (*Vitex trifolia* var. purpurea): An evidence of season effects.

Foods 2019, 8(2), pii: E52.

(IF: 3.01, Q2)

6. Barfroshan Y, **Mottaghipisheh J**, Maghsoodlou MT, Dosti N, Beyzaei H, MoghaddamManesh M, Vitalini S, Iriti M.

Comparative study of bioactivities and chemical constituents of *Cymbopogon jwarancusa* subsp. *olivieri* (Boiss.) Soenarko harvested in spring and winter.

Journal of Essential Oil-Bearing Plants 2018, 21(4): 1107-1118.

(IF: 0.68, Q3)

7. Mottaghipisheh J, Ansari Moghaddam M, Valizadeh J, Maghsoudlou MT, Iriti M.

Essential oil constituents and biological activities of leaf extracts of *Semenovia suffruticosa* from Iran.

Records of Natural Products 2017,11(4): 395-400.

(IF: 1.2, Q2)