ENCAPSULATION OF EXTRACTS FROM MIDDLE EAST MEDICINAL PLANTS AND ITS ADVANTAGES – A REVIEW ARTICLE

FAEZEH FATHI,[*] SAMAD N. EBRAHIMI,[*] FERNANDO ROCHA[**] and BERTA N. ESTEVINHO[**]

[*]*Department of Phytochemistry, Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, Iran*
[**]*LEPABE – Laboratory for Process Engineering, Environment, Biotechnology and Energy, Faculty of Engineering, University of Porto, Dr. Roberto Frias Str., 4200-465 Porto, Portugal*
✉ *Corresponding author: B. N. Estevinho, berta@fe.up.pt*

Received January 22, 2021

Medicinal plants have played an important role in the development of human health care and culture, serving as both medicine and food. Herbal drugs have been used for centuries for the treatment of several diseases and many of the new medicines are produced based on recent research on their traditional uses. Medicinal plants of the Middle East are regarded as a rich resource of different valuable bioactive compounds. Such compounds extracted from natural resources maintain many potential health benefits. The application of bioactive compounds is, however, rather limited in food and drug formulations because of their poor bioavailability, fast release and low solubility. Thus, encapsulation can protect the bioactive compounds from environmental stress, improve their physicochemical functionalities, reduce the potent toxicity of drugs, modify the release of encapsulated active materials, reduce dosage, enhance their health-promoting and anti-disease activities.
This review discusses the importance of the pharmaceutical properties of thirty-two species of relevant medicinal plants native to the Middle East and their uses in various industrial applications.

Keywords: bioactive compounds, encapsulation, encapsulating agent, herbal drugs, medicinal plant, natural product

INTRODUCTION

The World Health Organization (WHO) indicates that there are 20,000 different medicinal plants reported in more than 91 different countries that have adequate weather conditions for plant growth.[1] Determining the plants that can be candidates for pharmaceutical research, including their compounds of interest, among a large number of potentially valuable natural bioactive compounds, is a particularly challenging process. It would require important skills and consideration of different market-related aspects, including the comprehensive procedures for extraction and product elucidation and characterization.[2,3]

Secondary plant metabolites are bioactive natural products that can have important benefits for human health. Data on plant extracts, summarized after an overview of numerous studies published in the last two decades, revealed the potent properties of natural products, highlighting the importance of several classes of compounds, such as monoterpenes,[4,5] monoterpene hydroperoxides, bicyclic monoterpenes, diterpens, tetranortriterpenoids,[6] sesquiterpene,[4,5] sesquiterpene coumarins,[7] triterpenoids,[8] polysaccharides,[9] phenolic compounds,[10–12] phenolic acids,[12,13] flavonoids,[14,15] flavonoid anthocyanins,[14-17] carotenoids,[5,16,18] tannins,[13,15] coumarins,[15,17,19] ocopherols,[12] steroids,[13,15,17] saponins,[13,15,17] alkylamides,[20] alkaloids,[15,17] tropane alkaloids,[21] isoquinoline alkaloids, pyrazole alkaloids,[22] pyrrolizidine alkaloids, acridone alkaloids,[6] anthraquinone, naphthoquinones, glucopyranoside, naphthalene, xanthones,[23] proteins, resins, fiber, ash,[9] amino acids,[24] Na, Mg, Ca, K, P, Mn,[9] vitamins,[24] and a wide range of phenolic acids, for instance, rosmarinic acid,

ellagic acid, palmitoleic acids, linoleic acid, chlorogenic acid, caffeic acid, ferulic acid, p-hydroxybenzoic acid, gallic acid, vanillic acid, syringic, p-coumarin acid, caffeic acid,[25] among others. Numerous available plant species have a potential application in the food and pharmaceutical industries for the production of generally used pharmaceutical drugs and foods for human consumption, including capsules, health supplements, energy drinks, energy boosters, food products, nutraceuticals *etc*.

This work reviews some of the most important medicinal plants used in the Middle East that have shown clinical efficiency in the treatment of different kinds of diseases, and discusses possible uses of these plants in the pharmaceutical, food and cosmetic industries. Moreover, the advantages of encapsulating various plant extract bioactive compounds, by different techniques, for controlled release or drug delivery applications, which would affect the performance of the final product and its efficiency, are discussed.

RELEVANT MEDICINAL PLANTS IN THE MIDDLE EAST

In this section, the main relevant medicinal plants grown and used in the Middle East, namely in the region of Iran, will be presented. These medicinal plants have had several applications during centuries in the human diet, some for food or medicine, and others as spices, to preserve food products, fruits, *etc*. Their composition, biological activities, traditional uses, some of their health benefits and risks will be discussed. Some of these plants can be medicine or poison, depending on the amount of plant ingested. Their application as nutraceuticals and as bioactive food products is a challenge.

Satureja khuzistanica is an endemic aromatic medicinal herb of the Lamiaceae family that grows in Iran. The local people believe that it reduces cholesterol, controls the heart rate, blood pressure and rheumatic pain, and helps in losing weight. The essential oil of *S. khuzistanica* contains carvacrol, thymol, and a number of other phenolic compounds, as well as vitamins B, C, A and niacin. There are several reports on the antimicrobial and antioxidant properties of its essential oil, which are due to the presence of carvacrol. Carvacrol is a famous compound for many diverse biological activities, including antimicrobial, antitumor, analgesic, anti-inflammatory, antiparasitic, antihepatotoxic and hepatoprotective activities.[26] Further, *S. khuzistanica* has antifungal,[26,27] antidiabetic, hypoglycemic, antihyperlipidemic, anticholeretic, scolicidal, lysozyme activities and hematological factors.[28–30] On the other hand, traditional medicine says it may affect the lungs if overused.[26,28,29]

***Crocus sativus* L**. belongs to the Iridaceae family and is widely cultivated in Iran. Actually, Iran is the world's leading producer of saffron. It contains quercetin, galangin, kaempferol, chrysin, rosmarnic acid, naringenin, pinocembrin, myricetin.[31] The chemical compounds found in saffron, such as crocin, crocetin (carotenoid), safranal,[18,19,32] and its phenolic compounds[10,11] have several significant properties described in traditional medicine, being used for alleviating sunburns, improving sexual function, reducing menstrual pain, and considered beneficial for the health of liver and kidney. Many scientists reveal that C. *sativus* has antioxidant, antimicrobial,[10,31] anticancer, antigenotoxic, anti-apoptotic, angiogenesis, anti-Alzheimer, anti-Parkinson, anti-convulsant, anti-depressant, anti-inflammatory, and anti-diabetic activities. It also has positive effects in the case of myocardial infarction, the nephritic syndrome, lipid peroxidation, thrombosis, respiratory disorder, insulin resistance, ischemia and anxiolytic visual impairment.[11,33] *C. sativus* extract has been investigated for the treatment of colorectal cancer.[18,19,34] The most important constituent of C. *sativus* is saffron, and most of the medicinal uses of this species are due to it. The production of 1 kg of saffron uses almost 150.000 flowers. So, contemplating the number of flowers used to obtain the desired amount of saffron, the amount of petal waste, which are considered a by-product, can be deduced.[35]

***Zataria multiflora* Boiss**. belongs to the Lamiaceae family and mainly grows in Iran, Pakistan and Afghanistan.[36] It is used traditionally for medicinal purposes due to its antiseptic, analgesic, carminative and intestine-soothing activities.[37] It is used in folk medicine to treat various ailments, such as cramps, muscle pain, nausea, indigestion, diarrhea, and cough.[38] Z. *multiflora* is a good source of rosmarnic acid and has p-cymene, carvacrol, thymol, and methyl-5-(1-methylethyl)-phenol. Different pharmacological aspects have been described for this plant, including its antioxidant,[39,40] antimicrobial,[37,40,41] cytotoxic, anti-inflammatory, anti-cancer,[42] anti-ulcer,[43] and COPD activities.[36,44,45] It is also recommended for the

treatment of fatty liver disease[46] and hydatid disease,[47,48] being also recognized for its wound healing, spasmolytic, antifungal,[49] anti-nociceptive,[50] and expectorant activities.[51] *Z. multiflora* does not have any significant toxicity and has wide application in the herbal pharmaceutical industry.[37]

***Froriepia subpinnata* Baill**. is a medicinal herb and endemic vegetable, which grows naturally in the north of Iran. *F. subpinnata* has 150 species native to Eurasia and Africa, and more than 16 species to Europe. *F. subpinnata* grows in Central, West, and North of Iran and especially at high altitudes with a cold climate.[52] In folk medicine, it has been used as carminative, appetizer, antiseptic, antispasmodic, anti-diuretic, sedative, and galatogogue agent.[52,53] Some pharmacological research on *F. subpinnata* has been reported, revealing that its essential oil has anti-cancer activity,[52,54] as well as antioxidant,[53] and antibacterial activities.[52,54]

***Hyssopus officinalis* L**. is one of the most important plants from the Lamiaceae family, being considered a medicinal plant and cultivated in regions of Asia, Europe and America. The aerial parts of *H. officinalis* have been traditionally used in the treatment of infections due to its antiseptic properties. In addition, it is stimulative, carminative, expectorant, antispasmodic, being used for the cure of colds, cough and asthma.[55] H. officinalis contains 1,8-cineole,[55,56] α-glucosidase,[57,58] cis-pinocamphone, pinocarvone, caffeic and chlorogenic acid.[59,60] The essential oils obtained from Iranian H. officinalis have moderate antioxidant properties, but great antibacterial activity. The essential oil can be used as a natural antimicrobial agent, being effective for the inhibition of bacterial growth of different strains, especially Escherichia coli. The antibacterial and antioxidant activities of these essential oils could be partly due to the presence of some classes of compounds, such as monoterpene ketones, hydrocarbons, and oxides. Some studies recommend the use of the natural antibacterial and antioxidant agents derived from *H. officinalis* for application in the food industry.[56] Its antibacterial and antifungal properties have been also attributed to the presence of pinocamphone and isopinocamphone. The antiviral effect of the plant is probably due to the presence of caffeic acid, tannins, and unknown high molecular weight compounds.[61,62] Other studies also report on its antioxidant, antibacterial,[56,59,63] antidiabetic,[57] anthelmintic[64] and antifungal activities.[59] It has drawn attention for the treatment of chronic bronchitis and asthma,[65] as well as due to its strong antiviral activity against HIV.[61,66]Also, due to its content of α-glucosidase inhibitors, *H. officinalis* could be used to prevent and treat diabetes.

***Curcuma longa* L**., also called turmeric, belongs to the Zingiberaceae family and is highly valued worldwide due to its medicinal and economic significance. More than 100 active compounds are found in this herb. The root contains volatile oils, such as tumerone, and coloring ingredients, known as curcuminoids.[27] The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane), and its various volatile oils, including tumerone, atlantone, zingiberone, zingiberene, α-phellandrene, cineol, sabinene, borneol, sesquiterpene, monoterpene,[4,5] carotenoids and polyphenol compounds.[5] *In vivo* and *in vitro* studies have shown that *C. longa* has significant pharmacological effects. In folk medicine, turmeric is used for respiratory diseases, such as allergies, liver problems, sinusitis and anorexia.[4,67] *C. longa* is a good source of proteins, carbohydrates, fiber, and ash, and contains a considerable amount of Na, Mg, Ca, K, P, and Mn. Fresh and dried turmeric leaves present low nitrate levels, with no cyanogenic compounds, which makes their consumption safer for the consumers.[9] A special emphasis was also given to the activity of curcumin in the case of intoxications and multiple malignant diseases.[68] In general, different studies have revealed that *C. longa* has anti-inflammatory,[4,69] antioxidant,[4,5,70] antitumor, antimicrobial, antitoxin, gastro-protective,[4,71,72] and anti-carcinogenic[69] activities in the case of oral cancer, skin cancer and stomach cancer.[4,73,74] It presents cyclooxygenase enzyme activity,[75,76] and cardio-protective effects.[77] It has been also reported to have hepatoprotective, antiarthritic and hypoglycemic properties.[78,79] *C. longa* has been examined for its benefits in the case of neurodegenerative diseases and for wound treatment.[4] It has been established that this plant rises dopamine, norepinephrine and 5-HT levels in the central nervous system.[80] It demonstrated inhibition effects on apoptosis, platelet aggregation, cytokines production, reactive oxygen species production, oxidative brain damage, cytokines production, cognitive deficits in cell culture and animal models.[75,76] *C. longa* has antifungal activities against

Trichophyton longifusus,[81] and is antibacterial.[82] Clinical trials proved the positive effects of curcumin on inflammation, skin, eye, central nervous system, respiratory, cardiovascular, gastrointestinal, urogenital and metabolic disorders.[68,83,84] Braga *et al*. have cautioned that the plant could have nitrate toxicity.[9]

Ferula assa-foetida **L**. belongs to the Umbelliferae family and is a medicinal plant native to Iran, India and some regions of Afghanistan.[7] There are two types of it: bitter and sweet. The plant is traditionally used for the treatment of different diseases, including asthma, epilepsy, intestinal parasites, influenza,[85] and to alleviate toothache.[86] In Iranian traditional medicine, it has been used as an antispasmodic and carminative agent, and – due to its anthelmintic effect – for the treatment of bronchite vermineuse[87] and intestinal parasites.[88] *Ferula assa-foetida* is also known as "Anghouzeh", "Khorakoma" and "An-guzakoma" in Iran.[89,90] The plant contains various chemical constituents, such as beta-pinene, E-caryophyllene, elemicin, cedrol, myrcene, ferulenol, ferulenol acetate, carvacrol, thymol, ferutinin, jaeschkeanadiol vanillate, kuhistanol D, kuhistanol A, (E)-1-propenyl sec-butyl disulfide, 1-(1-propenylthio) propyl methyl disulfide, and 1,2-di-thiolane.[90,91] It is a good source of sesquiterpene coumarins.[7] *F. assa-foetida* has been proved to have antimicrobial, antifungal, antibiofilm,[85,90] antidiabetic and antihyperlipidemic effects,[92] as well as antitumor,[93] sedative, diuretic, and emmenagogue activities.[94] It is a potential source for developing novel antimicrobial agents in order to control fungal and bacterial infections or to improve the quality and extend the shelf life of food products.[90]

Datura stramonium **L**., belonging to the Solanaceae family, produces pharmaceutically important tropane alkaloids, including scopolamine and hyoscyamine, potent antagonists of the acetylcholine receptor[95] and have been used as a taxonomic criterion in chemotaxonomy studies.[21] In recent years, *D. stramonium* has been used as a recreational drug due to its hallucinogenic and euphoric effects.[21] Different alkaloids are obtained from the plant for medicinal purposes, to be used in the treatment of various groups of diseases, especially of the respiratory and muscular-skeletal systems. Several studies investigated the pharmacological activities of *D. stramonium*. It has been proven to have anti-proliferative activity against human gastric adenocarcinoma and potential immunosuppressive effects,[96] cytotoxic activity in carcinomas of colon, breast and lung,[97] anticholinergic properties.[21] It treats inflammation of the UVA and Parkinson's and painful spasms, promotes cyclopegia in cases of accommodative strabismus, and prevents motion sickness.[21] It has antitumor and antimitotic activity.[98] Some authors propose the following mnemonic rule to remember the symptoms produced by poisoning by *D. stramonium*: "blind as a bat, mad as a hatter, red as a beet, hot as a hare, dry as a bone, bowel and bladder lose their tone, and the heart runs alone".[95,99]

Ficus carica **L**. belongs to the Moraceae family, represents one of the greatest plants in this genus of angiosperms, which comprises more than 800 species of trees cultivated in tropical and subtropical areas, and it traditionally used for constipation, cough problems, piles, and diabetes. It treats the foot and mouth disease in livestock.[100] The main ingredients of *F. carica* are flavonoids, phenolic acids, phenolic compounds, anthocyanin,[100] tannins, alkaloids, glycosides, coumarins, triterpenoids, sterols and vitamin E.[101] It also includes ficusin, vitexin, alpha-amyrin acetate, isovitexin, kaempherol, quercetin, naringenin, and blacalein.[101] It presents anti-diabetic, anticancer, anti-inflammatory,[101,102] and antibacterial activities,[103] and treats atopic dermatitis[103] and constipation[105,106] in pediatric patients. It has been demonstrated to have antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa* and *Escherichia coli*.[103,107,108]

Artemisia absinthium **L**., from the Asteraceae family, generally known as wormwood, it is a perennial herb with fibrous roots, growing on non-cultivated, dry ground or rocky slopes and at the edge of footpaths and fields. It is usually used as an ingredient in the spirit absinthe, and as a flavoring agent in some other spirits and wines.[109] In folk medicine, it has been used for various infectious diseases, Crohn's disease or as an antimicrobial agent,[110] it has also proved a hemorrhoid healing effect.[111] The main ingredients of *A. absinthium* are phenolic compounds,[112] acyclic monoterpenes, monoterpene hydroperoxide, bicyclic monoterpene, glycosides,[113] β-thujon, p-cymene, β-pinene and ethyl-5,6-dihydro-1,4-

dimethylazulene.[114] Many investigations on *A. absinthium* proved that it has anthelmintic,[64,114,115] antimicrobial,[116,117] antioxidant,[114,118] anti-feedant, anti-venom,[119] and antitumor activities,[120] as well as hepatoprotective[117] and neuroprotective effects,[121] and with benefits in the case of cutaneous lesions.[122] The plant has been demonstrated to have antiprotozoal effects against *Leishmania aethiopica* and *L. donovani*, as well as acaricidal, insecticidal and fungicidal activities.[116,117]

***Bunium persicum* (Boiss.) B. Fedtsch**. relates to the Umbelliferae family. Also called Kala zeera, it is a high-value herbaceous spice generally used for culinary, flowering, perfumery and carminative puposes.[123] *B. persicum* is a rich source of alkaloids, flavonoids, steroids, glycosides, phenols, saponins, terpenoids, and tannins.[13] It is rich in cumin aldehyde and ɣ-terpinene, and also has trans-3-caren-2-ol, acetic acid, terpinolene, 1,3,8-p-menthatriene, hinokitiol (β-thujaplicin), estragole, pulegone, limonene, methyl eugenol, and bornyl acetate.[124] Its large amount of phenolic compounds, specifically, flavonoids, can explain its excellent antioxidant activity.[13] γ-Terpinene, cumin aldehyde, ρ-cymene and limonene cause high antimicrobial and antioxidant activities.[125] *B. persicum* is a rich source of oils, with different biological activities, such as antioxidative and antimicrobial ones.[126] Several studies revealed that *B. persicum* has antioxidant,[13] antimicrobial, antifungal, larvicidal,[127] diuretic,[128] anti-tumor, antinociceptive,[129] antihematotoxic,[126] anti-inflammatory, antihistaminic, hypolipidemic, anticonvulsant, anticholinergic, antidiabetic and antidiarrheal[125] activities. Also, it has been demonstrated to have apoptotic activity on human leukemia cell lines.[130]

***Nigella sativa* L.**, known as black cumin, is an annual flowering plant of the Ranunculaceae family, native to south and southwest Asia. Ancient people believed that it increased male potency and improved intelligence and memory,[131] being also used to treat infertility, epilepsy,[132] and liver disorders.[132] *N. sativa* has two classes of alkaloids, including isoquinoline alkaloids, such as nigellimine-N-oxide, and pyrazole alkaloids, such as nigellidine and nigellicine,[22] and also has proteins and saponins.[133] It also contains different compounds, such as thymoquinone, thymol, limonene, carvacrol,[134,135] α-pinene, 4-terpineol, longifolene, t-anethole benzene, trans-anethole, alpha-thujene, anisaldehyde, n-nonane, miristicine, sabinene, fenchene, apiol.[134,136] Thus, it has proven effective anthelmintic, antiviral, antibacterial, antipyretic,[137,138] moderate anti-mycotic,[139] anti-hyperglycemia, anti-hyperlipidemia,[140,141] anti-inflammatory, anti-oxidative,[142,143] anti-cancer and anti-hypertensive activities.[137] Several studies[142–144] have reported on its carminative and blood sugar lowering effects,[138] wound healing,[137] and ameliorating effects in the case of metabolic disorders.[140,142] It has been found to bring benefits in rheumatoid arthritis, asthma, diabetes and digestive diseases,[117] in addition to decreasing the water intake in rats with STZ-induced diabetes.[143,145]

***Cuminum cyminum* L.**, belonging to the Umbelliferae family, is used in folk medicine as a stimulant, carminative and astringent agent, in cases of flatulence and diarrhea, and as a remedy against indigestion. It is also used to flavor foods and other products.[37,41] It is a rich source of phenolic compounds, anthocyanins, flavonoids, alkaloids, coumarins, anthraquinone, glycoside, proteins, resins, saponins, tannins, steroids,[15,17] cuminal, and cumin alcohol.[17] Its essential oil contains pinene, cineole, linalool,[51] carrvone and cumin aldehyde.[147] Many scientists revealed that *C. cyminum* has antioxidant, antifungal, antimicrobial,[17,37,146] antitumor, anti-inflammatory,[148] antihypertensive, hypocholesterolemic, antidiabetic and diuretic effects,[149] also being beneficial to inhibit platelet aggregation, as a bronchodilator, immunological, contraceptive, anti-osteoporotic,[17,139] anti-diarrheic, and antispasmodic agent.[51] Due to its benign activities, it is used in the treatment of mild digestive disorders, bronchopulmonary disorders,[150] intestinal inflammation,[148] abdominal pain and bloating, as well as to heal fractures and body aches.[131] Besides these, it also used for preserving various food products.[146] Moreover, *C. cyminum* does not have any significant toxicity and therefore has been considered as an efficient alternative to conventional antimicrobial agents to be included into packaging materials that come in contact with foods.[37] As the extract of *C. cyminum* contains many sensitive compounds, which can easily suffer degradation in the presence of oxygen, light and moderate temperatures, it has been a challenge to stabilize essential oil formulations.[146]

***Glycyrrhiza glabra* L.** belongs to the Fabaceae family, and is among the oldest and most widely

used spices and medicinal plants in both Eastern and Western countries, especially in Iran and Europe.[151] It has been used for the treatment of chronic hepatitis for more than 60 years in Japan, and also has therapeutic benefits against other viruses; it presents expectorant, anti-tussive, mild laxative, and anti-aging activities.[152] *G. glabra* is a good source of flavonoids, alkaloids, steroids, terpenoids, saponins, tannins, glycosides, and triterpenoid saponins.[8] The primary bioactive compounds of *G. glabra* have anti-androgen and phytoestrogen effects,[153] also presenting anti-coagulant,[154] anti-bacterial, anti-inflammatory, antiulcer, free and hydroxyl radical scavenging, anticonvulsant, and anxiolytic activities.[8,155] *G. glabra* has been used to treat coughs, bronchitis, constipation, gastric ulcer,[143,156] and stomach pain, joint pain (back and leg), bone fractures,[131] and stomach infection.[148,156] Its anti-inflammatory effect occurs by inhibiting the migration of white globules and the production of inflammatory meditators and neutrophils.[157]

***Dracocephalum moldavica* L**. is an annual aromatic plant belonging to the Lamiaceae family. *D. moldavica* has been investigated due to its naturally present components, such as germacrene, caryophyllene, α-copaene, δ-cadinene, ethyl nerolate, rosmarinic acid and phenolic compounds, such as luteolin and apigenin.[158,159] Rosmarinic acid and phenolic compounds cause antioxidant,[158,160] and antifungal activity.[161]

***Arctium lappa* L**. belongs to the Asteraceae family. Commonly known as burdock, it has been widely consumed as a vegetable and due to its medicinal properties in East Asia for centuries.[162] *A. lappa* has been traditionally used for the treatment of acne, dermatitis, diffuse skin telangiectasia (hepatic diseases), skin infections, purulent wounds, furuncles, venereal diseases, hyperhidrosis, skin inflammation, mouth diseases, alopecia and dry scalp seborrhea. *A. lappa* contains many interesting compounds, such as amino acids, nucleotides, vitamins, flavonoids, terpenoids, polyphenols, oligosaccharides, polysaccharides, and polyunsaturated fatty acids.[24] Due to its composition, *A. lappa* has a wide range of medicinal properties, such as anti-inflammatory,[164,165,170] anti-burning sensation, anti-infective, depurative, hemostatic, hair tonic, analgesic,[164] anticancer, antidiabetic, antiviral,[163] antibacterial against both Gram-positive and Gram-negative bacteria,[166] and hepato-protective effects.[167,168] The plant has been utilized in the treatment of different cancer types (breast, ovary, bladder, pancreas), malignant melanoma and lymphoma. It has been established that it relieves the pain, lessens the tumor size and enhances the survival phase.[163] *A. lappa* was also assessed due to its anti-mutagenic properties in lung, kidney, brain and testicles tumors. Most studies on the bioactivities of A. lappa have focused on its low molecular weight phytochemicals, such as arctigenin, arctiin, tannin, β-eudesmol, caffeic acid, chlorogenic acid, lappaol and diarctigenin.[169] The synergistic anti-inflammatory and protective effects of the associated A. lappa extracts were investigated in the management of the inflammatory response in a COPD model.[165]

***Punica granatum* L**., known as pomegranate, is a fruit-bearing shrub belonging to the Punicaceae family. It is native to Afghanistan, China, Iran and India, but it is also cultivated in the Mediterranean region.[171] The fruit is widely used in making juice, despite some concern about its inedible part, the peel, which represents approximately 77%. Pomegranate peel is popularly used as traditional herbal medicinal products. It is a rich source of tannins, flavonoids, polyphenols, and some anthocyanins, as delphinidins and cyanidins.[172] Several studies demonstrated that pomegranate peel has significant anti-infective, anti-oxidative, antimicrobial, anti-atherogenicity, hepato-protection, antidiarrheal, anti-atherogenicity, and anti-mutagenic characteristics.[173] It is a potential agent for the treatment or prevention of inflammation and cancer.[174] Polysaccharides from pomegranate peel have antioxidant and hepato-protective activities.[173] Pomegranate has anti-urolithiatic and cardiovascular protection roles.[175,176] The antibacterial[172] properties of pomegranate peel in *in-vitro* model systems have been reported. Pomegranate fruit powder was found to stimulate the cell-mediated and humoral components of the immune system in rabbits, at the dose of 100 mg/kg, administered orally as aqueous suspension. Pomegranate additionally improved the inhibition of leucocyte migration in leucocyte migration inhibition tests and induration of skin in delayed hypersensitivity tests.

***Lawsonia inermis* L**., known as Henna, belongs to the family of Lythraceae and is a well-known antimalarial medicinal plant.[177] Henna is widely used by cosmetics manufacturers.[178] Its leaves have been widely used as a dye for hands, feet, hair, and textiles.[178] Henna is a good source

of coumarins, naphthoquinones and a variety of flavonoids,[23] several types of acacetin, luteolin, apigenin, appin, cosmossin, isoscutellarin, lawsochrysin and catechin. It is also a precious source of volatile and non-volatile terpenes. Lawsaritol steroids and two alkaloids named harmine and harmaline have been also found in henna.[23] Several researchers have investigated the plant's pharmaceutical properties. They revealed that it has antimicrobial,[179,180] anticancer,[181,182] antibacterial,[23] antimalarial,[177,179] antiviral,[183] antifungal against human pathogens,[184] antidiabetic, anti-inflammatory,[181] antioxidant,[178,181] anti-ulcer, anti-tubercular,[185] and hepatoprotective,[186] activities. Henna has a potent activity of wound healing.[23,187,188] Henna has the capacity of preventing linoleic acid oxidation,[189] moisture loss, skin cracking, chronic ulcers and discomfort in the feet of diabetics.[23] Henna also contributes to enhancing memory.[23] An acute toxicity study of henna carried out in Sprague-Dawley rats proved the median oral lethal dose as above 2000 mg/kg.[190]

***Ziziphus Jujuba* Mill**. belongs to the Rhamnaceae family and is widely distributed in the subtropical and tropical regions, particularly in Australia, southern and eastern Asia, and Europe.[191] Diverse active ingredients were found in it, such as polysaccharides,[191] oleic, linoleic, palmitic, palmitoleic,[25] p-coumaric, cinnamic, caffeic, chlorogenic, ferulic, p-hydroxybenzoic and vanillic acids, as well as quercetin, rutin, quercetin-3-galactoside, quercetin-3-rutinoside, kaempferol-glucosyl-rhamnoside, epicatechin, catechin, and procyanidin B2.[25] Many investigations have revealed its antifungal, antibacterial, antioxidant, anti-ulcer, anti-tumor, anti-stress, hepato-protective, hypoglycemic, anti-inflammatory, sedative, cytotoxicity, immune-stimulating, gastrointestinal protective,[191,192] and anti-insomnia activities.[193]

***Pimpinella anisum* L**. belongs to the Apiaceae family, and is a medicinal and aromatic plant widely cultivated in Asia, and the Mediterranean area. *P. anisum* is among the most extensively used plants for infant healthcare. Traditionally, it has been used as carminative, expectorant, sedative, antidepressant, insecticidal, antiviral, antispasmodic, nematocidal, mutagenic, diuretic, estrogenic, antimalarial, and pectoral stimulant. It has been reported for the treatment of abdominal pain and flatulence. Other woks reported on its antioxidant, antiseptic,[58,194] anti-inflammatory,[194] analgesic, antifungal, anti-diabetic and anti-convulsing activities. Enzyme inhibitory or stimulant, and hypothermic activities are the other most important effects of the plant. Moreover, *P. anisum* is used in the treatment of renal colic, intestinal colic, and upper respiratory tract problems,[195] for the treatment of gastrointestinal disturbances, bronchial asthma, insomnia, persistent cough, and epilepsy.[100]

***Artemisia dracunculus* L**., commonly called tarragon, belongs to the Asteraceae family, and consists of around 500 species distributed all over the world. The composition and biological effects of the essential oil (EO) of *A. dracunculus* have been widely studied. In Iranian folk medicine, it is used as an antiepileptic, anticonvulsant, and sedative agent, these effects being related to the presence of monoterpenoids.[196] The major constituents are sabinene and estragole, as well as alkamides, pellitorine, neopellitorine A, and neopellitorine B.[20] Estragole is responsible for the genotoxicity and carcinogenicity activities of the oil.[197] Tarragon has been extensively used in traditional medicine and as part of the human diet for centuries. Its medicinal uses are also related to its moderate antimicrobial inhibitory effect, anticoagulatory, antihyperlipidemic,[198] anti-diabetic,[196,199] antifungal, allopathic and insecticidal activities.

Citrus aurantium and ***C. aurantiifolia***, of the Rutaceae family, like most of the *Citrus* genus, are native to tropical and subtropical Southeast Asia. *C. aurantium*, or bitter orange, is traditionally used for consumption. It has been reported to contain coumarins, limonoids, flavonoids, tetranortriterpenoids, monoterpenoids, and acridone alkaloids.[6] Limonene, acriquinoline A and acriquinoline B have been found to be the major constituents of its essential oil.[6] Other studies have also mentioned the presence of citpressine I, citpressine II, citruisinine II, citracridone II, 5-hydroxynoracronycine, 8-hydroxy-6-methoxy-3-pentylisocoumarin, xanthyletin, clausarin, (E)-suberenol, transgleinadiene, methoxysuberenol, fridelin, lupeol, limonin, stigmasterol, β-sitosterol, and β-sitosterol-3-O-β-D glucoside in *C. aurantium.*[200] A number of authors have established its beneficial health effects, including its antioxidant,[201,202] anti-inflammatory,[201-203] anticancer,[203,204] antiseptic, antispasmodic, aromatic, astringent, carminative,[203] cytotoxic, antimalarial, antimicrobial, anti-allergic, anticonvulsant properties and antiplatelet aggregation activity.[205,206]

The acetyl group in the phenolic compound plays an important role in its antioxidant activity and the cytotoxicity activity against NCI-H460 and CAL-27 cell lines.[202] Also, herbal supplements with *C. aurantium* are recommended due to its slimming effect.[203,204] It has also been used in treating anxiety and other central nervous system disorders,[207] gastrointestinal disorders, insomnia, headaches, cough, muscular pain, nausea, ringworm infection and hypertension.[203]

C. aurantiifolia is traditionally used as food flavoring and as facial wash to rejuvenate the skin. The most important secondary metabolites include limonoids, rhamnose, arabinose, galactose, glucose, mannose, and galacturonic acid.[208] Its antimicrobial,[209,210] antiviral,[208,209] anti-tumor, anti-carcinogenic, immunomodulation, analgesic, anthelminthic, anti-mutagenic,[211,212] and antifungal[213] activities have been reported. *C. aurantiifulia* has been found to inhibit human pancreatic cancer cells and viral infection.[214] Limonin, present in *C. aurantiifulia*, has been shown to possess anti-carcinogenic properties in *in vivo* rodent models, demonstrating cytotoxic activity.[208] Also, it reduced the incidence of 7,12-dimethylbenz(*a*)anthracene (DMBA) induced buccal pouch epidermoid carcinomas in female Syrian hamsters.[212]

Echium amoenum **Fisch**. **& C**.**A**. **Mey**. is known as Iranian borage and is a member of the Boraginaceae family. There are 4 species of the genus *Echium* growing in Iran, but only *E. amoenum* has medicinal uses. It also grows in most of Europe and in the Mediterranean region. The traditional medicine in Iran uses the plant as a remedy for cough, sore throat and pneumonia, due to its anti-inflammatory and analgesic effects, but also as an anxiolytic and sedative.[159,215] Pyrrolizidine alkaloids, such as echimidine, echimidine isomer, 7-angeloyl retronecine, 7-tigloyl retronecine and rosmarinic acid, were identified in this species.[159] Its antidepressant, demulcent, atonic, tranquillizer, and diaphoretic activities have been discussed.[216] Also, *E. amoenum* exhibited high inhibition capacity towards some key enzymes that are considered as triggering major health problems.[217]

Malva sylvestris **L**. species, known as common mallow, belongs to the family of Malvaceae.[218] It has strong antioxidant properties, including radical-scavenging activity,[12,219] as well as lipid peroxidation inhibition in liposomes. It is a good source of natural antioxidant compounds, such as phenols, flavonoids, carotenoids, tocopherols;[12] also, sesquiterpene, leucoanthocyanidines, anthocyanidines, coumarins, and anthocyanin have been reported.[220] *Malva sylvestris* possesses bacteriostatic, antinociceptive, and anticholinesterase activities; it is used in the treatment of inflammation, urinary, digestive, and respiratory disorders.[205] Young leaves are used for skin injuries, burns, diarrhea and stomach disorders, as well as rheumatism; shoots – for toothache, genital tract diseases, hemorrhoids and constipation; leaves and flowers – for colds, cough, sore throat, tonsillitis, bladder dysfunction and rheumatism; and finally, seeds are used for skin inflammation.[12] In general, the plant extract has cardioprotective,[221] anti-inflammatory,[222] and anti-psoriatic activities,[222] being also used for the treatment of colitis and stomatitis.[223] High amounts of ascorbic acid, carbohydrates and particularly sugars, such as fructose and glucose, were revealed in mallow. Further, the presence of malvidin 3-glucoside, scopoletin and quercetin suggested its anti-inflammatory activity.[224]

Boswellia serrata **Roxb**. **ex Colebr**. belongs to the family of Burseraceae.[225] Traditional Uman and Chinese medicine believes that it contains anti-inflammatory, analgesic, antihyperlipidemic, anti-bacterial and sedative substances.[226] Pentacyclic triterpenoids, tetracyclic triterpenoids and macrocyclic diterpenoids are the main constituents of Boswellia.[226] Several investigations have demonstrated its anti-inflammatory,[225,227,228] anti-arthritic,[228] hypolipidemic, immune-modulatory and anti-tumor activities.[225] It also has moderate hepato-protective activity against D-galactosamine-induced HL-7702 cell damage.[226]

Fraxinus excelsior **L**. belongs to the Oleaceae family and is a major charismatic tree species in Iran, Ireland, south Scandinavia and northern Spain.[229] Its phytomedicinal uses are due to its anti-oxidative,[230] anti-hepatitis, anti-ulcer,[230] anti-fibrotic, hepato-protective and liver regenerative,[231] anti-atherosclerosis, antimicrobial, anti-inflammatory, immunomodulation, hypocholesterolemic potential. It has been reported as a potent inhibitor of cyclic AMP phosphodiesterase activities.[230,231] *F. excelsior* is a potent source of glucoside, esters of hydroxyphenylethyl alcohols, lignans, flavonoids, simple phenolic compounds and coumarins, such as esculin and fraxin.[229] *F. excelsior* is also used for the treatment of rhinitis, stomatitis, toothache,

pyrexia and urinary organ infections in humans,[229] as well as fungal diseases in trees.[232]

***Ziziphus spina-christi* (L.) Desf**. belongs to the Rhamnaceae family, and is cultivated in sub-tropical and warm-temperate areas, all around the world, being commonly used in folk medicine for the treatment of various diseases. It has been found to contain nerolidol,[233] epigallocatechin, gallocatechin and spinosins,[234] saponins, phenolic compounds,[235] quercetin 3-O-robinobioside, quercetin 3-O-rutinoside, kaempferol 3-O-rutinoside, and quercetin 3-O-b-D-xylosyl-a-L-rhamnoside.[236] Several studies have revealed that it has anti-cancer and anti-inflammatory activities,[234] antibacterial, anthelminthic and antidiuretic properties, as well as cytotoxicity effects. Epigallocatechin, gallocatechin and sapinosins are responsible for the anti-inflammatory activities in natural extracts.[234]

***Myrtus communis* L.**, which belongs to the Myrtaceae family, is a green scrub typical of the Mediterranean region, which grows spontaneously in many countries. Flavonoids, such as myricetin, quercetin, catechin,[16,237] anthocyanins,[16,238] arabinogalactan, cyclitols, glucose, organic acids and oligosaccharides,[238] terpinolene, tannins, such as gallotannins,[16] and phenolic acids, such as gallic acid and caffeic acid,[16] have been reported for this plant. It has been established as having significant anti-inflammatory,[237] antifungal,[239] anti-hyperglycemic,[240] antiseptic,[241] antimicrobial, antiviral, antioxidant,[242,243] and anti-mutagenic activities.

***Silybum marianum* L.**, belonging to the Asteraceae family, is a valuable medicinal plant traditionally used as a remedy for liver diseases, gallbladder disorders,[244] and neurological disorders, including depression, and Alzheimer's disease.[245] The plant has been found to contain flavonoids, such as taxifolin, silychristin, silydianin, silybin A, silybin B, isosilybinin A, isosilybinin B, and most importantly, silymarin.[245] *Silybum marianum* is a good source of antioxidant,[246–250] anti-diabetic,[249] anti-aging,[250] anti-amnesic, anti-Alzheimer,[248] anti-hepatotoxic and chemo-preventive substances. It protects the liver from toxins and free radical scavenging,[247,251] and also has hypocholesterolemic effects.[246]

ENCAPSULATION OF HERBAL EXTRACTS

Encapsulation technology

Encapsulation is a promising technology that has recently attracted renewed scientific interest for extending its applications in many different domains, starting from the pharmaceutical industry,[252–254] to cosmetics and personal care products, the food industry, construction, textiles, chemistry, and agriculture.[255] The encapsulation approach has been applied to develop a significant number of novel products on several markets, including aromatherapy, agrochemicals, paints, coatings, colorants, adhesives, biocides, nutraceuticals, oil and gas, paper systems, electronics and imaging systems.

Encapsulation lies in coating different substances within another material. Different micro/nano encapsulation methods have been used in industrial applications.[256,257] The encapsulated material is commonly referred to as the inner phase, the core material or filler.[255,258] The encapsulating agent is known as the external phase, the shell, coating or membrane.[259–262] The core includes the active ingredient, for example, drugs, odors, biocides, vitamins, *etc*., while the shell isolates and protects the nucleus from the surrounding environment, and is often prepared from different biopolymers, as will be further discussed below.[263,264] The main reasons for encapsulation, in all industries, include the protection of the active ingredient, by the encapsulating agent, from oxidation or deactivation, caused by environmental conditions; the enhancement of the bioavailability of a natural product in the human body, especially in the gastrointestinal tract; the controlled and targeted release of encapsulated active compounds, and their increased stability. Encapsulation processes can have the following advantages: conversion of liquids to solids; safe handling of toxic materials; separation of incompatible materials; masking the organoleptic properties such as color, taste, odor of substances; reducing the potent toxicity of drugs; reducing drug dosage; providing targeted and sustained release of the active agent; improving adhesion, penetration and release of the active principles under physiological changes in pH and temperature.[265]

Therefore, encapsulation requires consideration of two main factors: first, the

selection of an appropriate encapsulating agent for the preparation of a suitable encapsulation system, and second, the selection of an appropriate encapsulation technique. Numerous techniques have been investigated to encapsulate natural active compounds extracted from medicinal plants for therapeutic purposes. The more commonly reported methods are shown in Table 1.

Nano/micro encapsulation

Considerable research efforts have been directed towards developing safe and efficient encapsulation techniques. Nano/microtechnology is a multidisciplinary area of research, including materials engineering, biotechnology, physics and pharmacy, among others, focusing on the development of structures of nano/micro-sizes. Nanocapsules have sizes ranging from 1 to 1000 nm, while microcapsules – from 1 to 1000 μm; they can have a multitude of forms, depending on the substances and techniques used to prepare them.[263,264] The pharmaceutical nanotechnology has allowed the development of innovative drug release systems, which resolved many of the issues related to the administration of conventional therapy.

Encapsulating agents

Encapsulating agents play an important role in the efficiency of delivery systems. Current investigations successfully reported new combinations of different biopolymers or new encapsulating agents to enhance the properties of encapsulation systems and improve the protection of the bioactive agent, with better encapsulation functionalities and enhanced release profile.[263] Many different materials have been investigated to develop encapsulating agents; they must be selected depending on the significant features required for each proposed use. The most commonly reported materials used for encapsulation in the food and pharmaceutical industries are polysaccharides, proteins, lipids, and other organic and inorganic materials, as tabulated in Table 2.

Emulsion systems have been used for the encapsulation and successful delivery of different compounds. Emulsifiers play a significant role in the preparation of emulsions, which is generally regarded as an essential procedure to improve the shape, size, texture, stability and target release.[266] Emulsifiers can be divided into two classes: artificial emulsifiers and natural ones. In recent years, natural emulsifiers have become more relevant in the food industry due to their non-toxicity, excellent accessibility, and plentiful sources.

Table 1
Most relevant encapsulation methods

Encapsulation method	Properties	Ref.
Anti-solvent precipitation	• Simple, comparatively cheap, simple scale-up, non-toxic, non-flammable and chemically stable	250, 272
Complex coacervation	• Uses two or more biopolymers; • Simple, high core loading capacity, high encapsulation efficiency and excellent control release	273
Electrospinning and Electrospraying	• Simple, versatile, cheap, non-thermal method, enhanced oxidative stability and controlled release profile	274
Emulsification (Emulsion/ nanoemulsion)	• Includes two main techniques: single emulsion (O/W-W/O), double emulsion (W/OW-O/W/O); • Good for encapsulation of both hydrophilic and hydrophobic structures; • Encapsulation efficiency of up to 48% and 40-80 nm particle size	276
Extrusion	• Used for hydrophilic and hydrophobic compounds, as well as oil; • Increases the bioavailability of poor-water soluble compounds, time controlled, thermoliable	277
Fluid bed coating	• Time-consuming technique, low cost, low operational cost, and high thermal efficiency; allows total temperature control; • Encapsulates solid core materials	258
Freeze drying	• Used for heat sensitive compounds, stabilizing nanoparticles, improves the stability of active compounds; better encapsulation efficiency; • Improves oral bioavailability, increases the solubility of a poorly soluble structure	278

Liposome/nanoliposome	• Can entrap a wide range of natural active compounds	256
Phytosome/ nanophytosome	• Enhances bioavailability; • Enhanced capacity to cross the lipid-rich biomembranes and reach circulation; • Enhances the absorption of lipid insoluble polar phytoconstituents; • Substantially greater clinical efficacy; • Phytosome shows better stability profile owing to the chemical bonds formed between the phosphatidylcholine molecule and phytoconstituents; • Widely used in cosmetics due to better skin penetration and high lipid profile	279
Solid dispersion	• Used for poorly water-soluble compounds (lipophilic); • Increases bioavailability, decreasing particle size, improving wettability	280
Spray drying	• Simple, rapid, improves the retention of heat sensitive compounds, improves the stability of most natural compounds; • Converts a suspension of colloidal nanoparticles into nanostructured powder	256, 281, 282
Sol-gel	• Based on the preparation of a solution, sol and gel, solidification and heat treatment of the organic and inorganic compounds, improves the stability of most enzymes; • Easily scaled up, even considering the tight cost-in-use; • Used for the immobilization of lipase enzymes within a phyllosilicate and vinyltriethoxysilane	263
Suspension cross-linking	• Droplets are fixed by covalent binding and converted to capsules; • Simple, rapid, improves the stability of most proteins and polysaccharides	263
Freeze spray drying	• Combination of spray drying and freeze drying; • More efficient than both methods; • High oral bioavailability and high thermal stability of natural compounds	283
Solid lipid nanoparticle (SLN)	• Improves the performance of poorly water-soluble bioactive compounds, solvent-free, long-term stability	284
Nanostructured lipid carriers (NLC)	• Improves the performance of poorly water-soluble bioactive compounds; • High drug loading, encapsulation efficiency, long-term stability, solvent free	285
Inclusion complexation	• Drying method, increasing bioavailability; formation of inclusion complexes in the solid and the solution states	286
Thermal gelation	• High encapsulation efficiencies (>90%), for both lipophilic and hydrophilic compounds; • Bioactive, non-toxic; can encapsulate different bioactive compounds	287

Table 2
Most frequently used biopolymers as encapsulating agents – categories and properties

Encapsulating agent	Properties	Ref.
	Polysaccharide-based	
Dextrins	• DE value of 20; different types (white dextrin, yellow dextrin, brown dextrin); • Water soluble and hydrolyzed starches; • Applied in encapsulation of water-insoluble flavorings and oils	288
Maltodextrin	• DE value of <20; • Hydrolyzed starch, highly water soluble (~70%) and low viscosity in solution; • Improves emulsifying characteristics, reduces the oxygen permeability of the wall matrix, enhances the bioactive retention and controls the release profile	282, 289, 290
β-Cyclodextrin	• Formulation structure with a hydrophobic cavity inside and hydrophilic external surface; • allows molecular inclusion; • complexes with poorly water-soluble molecules to enhance the molecular solubility	291, 292
Hydroxypropyl cyclodextrin	• Most abundant natural cyclodextrins, inclusion complexation behavior, highly affects the size, shape, hydrophobicity and the form of the guest molecule; • Improves the solubility, chemical stability and bioavailability of some poorly soluble compounds	293
Cellulose ~~Carboxymethyl~~	• ~~Water-soluble, a biodegradable and biocompatible derivative of cellulose;~~	294

	cellulose (CMC)	• Used for stabilizing, thickening, binding, tableting, and encapsulation of active compounds, to enhance stability and bioavailability of active compounds	
	Methylcellulose	• High solubility, efficient oxygen, and lipid barrier properties; • Excellent film-forming characteristics	294
	Cellulose ethers	• Water-soluble, offers masking of colors and undesirable tastes, protective wall membrane for the encapsulated core; • Protective wall membrane for the encapsulated core and enhanced aesthetical appearance	295
	Hydroxypropyl cellulose	• Water-soluble; • Good film-forming ability, acts as a wall to oil and fat	291
	Cellulose acetate	• Improves encapsulation efficiency	296
	Ethyl cellulose	• Only used in oral formulations, non-ionic, non-irritant, biocompatible and compatible with many celluloses and resins; • Water-insoluble, soluble in many organic solvents such as alcohol, ether, ketone *etc*. • Biodegradable, stable against light, heat, oxygen, moisture and chemicals, • Good flexibility and mechanical strength in a wide range of temperatures, non-swellable	297
Pectin		• Extracted from peels of citrus fruits; • Anionic and linear polysaccharides; • Non-toxic, not digested in upper gastrointestinal tract by gastric or intestinal enzymes and poorly soluble in such condition; • High retention of mangiferin in microencapsulated particles; • Improves the physicochemical stability; • Enhances the sustained release of lipophilic compounds	298–301
Chitosan		• Linear cationic polysaccharide; • Second most abundant natural biopolymer after cellulose; • Non-toxic, biodegradable, biocompatible, film forming and antibacterial characteristics; • Improved encapsulation efficiency and stability	301–303
Modified chitosan		• Water-insoluble, non-toxic, biodegradable, biocompatible, film forming; • Improved encapsulation efficiency and stability	256
Alginate	Calcium alginate Sodium alginate	• Non-toxic, biocompatibility, hydrophilic, linear anionic polysaccharide; • Rapid dissolution behavior at intestinal pH or the presence of sodium ion	304, 305
Gum	Arabic gum Xanthan gum Seaweed gum (carrageenan)	• Non-toxicity, biodegradable, biocompatibility, safe for the human body; • Potential capacity to encapsulate flavors, aromas, phenolic compounds, antioxidant agents and nutraceutical compounds	290, 306–308
Sucrose		• Good solubility in water, non-hygroscopicity, low cost; • Used as a matrix for encapsulation of food ingredients and long shelf-life at ambient temperature	309
		Protein-based	
Whey protein		• Usually used as hydrogel, nanoparticle system, conservation;	310–312

		• High encapsulation efficiency (around 100%) and loading capacity (about 100%)	
Casein		• Extracted from milk, includes α s1-casein, α s2-casein, β-casein, and κ-casein; • Low viscosity in solution, slight flavor, high nutritional value; • Very useful for encapsulation of hydrophobic compounds	313, 314
Gelatin		• Water retention and film formation ability, biocompatibility, biodegradability and fast release	315–317
Soy protein		• Emulsification, water binding potential, fat absorption and nutrient protection against oxidation	318
Cereal protein	Zein	• Known as prolamine and extracted from maize; • α, β, δ, Y zein types; • Water soluble, biocompatible, biodegradable, self-assembly, inherent hydrophobic property	319–321
	Wheat protein	• Contains gliadin and glutenin compounds; • Less water solubility, gel formation ability; • Potent ability and stability maintenance to encapsulate fish oil	322, 323
	Barley protein	• Contains hordein and gluten endosperm; • Excellent emulsification properties and highly hydrophobic; • Potential ability to encapsulate fish oil with high efficiency and high loading capacity	324, 325
	Potato protein	• Inexpensive and non-allergic; • Potent antioxidant activity, foaming, and emulsifying ability	326
	Amaranth	• Contains high protein, amino acid and prolamine content (safe for the human body); • Good emulsifying, foaming, gelifying, film-forming, water retention capacity, and low-cost material	327 327, 328
	Pulse protein	• Contained in peas, chickpeas, lupins, and lentils; • Good emulsifying, foaming and entrapping efficiency; • Rich in protein, iron, potassium, folate, and fiber; • Low in fat and cholesterol	329
		Lipid-based	
Soybean lecithin		• Less toxicity; • Excellent function, emulsification, film formation, and encapsulation; • Biodegradable, biocompatible, excellent stability, high protection; • Significantly improves oral bioavailability; • Self-assembling, emulsification, wettability; • Potent for encapsulating both hydrophobic and hydrophilic natural active compounds	330–332
Egg lecithin			
Phosphtidyl–	Choline		
	Serine		
Cholesterol			

Advantages of encapsulating natural compounds

The micro/nano encapsulation of natural active substances for controlled release or drug delivery applications is a promising approach for solving some of the significant problems inherent to such applications. The most suitable methods for encapsulating various natural products vary depending on the active compounds and the encapsulating agents used. Table 3 presents some of the most relevant studies on the encapsulation of different extracts from Middle East medicinal plants, detailing on the active agent, the encapsulation method selected and the encapsulating agent, as well as providing a brief explanation of the preparation procedure.

The research works included in Table 3 demonstrate the advantages of the encapsulation technology as applied to active compounds of medicinal plants. Thus, Kyriakoudi *et al*. reported on preparing *Crocus sativus* nanoparticles by the spray drying method, highlighting the advantages thus-achieved – an increase in the stability of crocins and picrocrocins under thermal and gastrointestinal conditions,[267] which can be beneficial for the application of saffron in the pharmaceutical and food industries. Another study also verified an enhancement in the bioavailability, bioaccessibility, and stability of saffron bioactive components by spray drying encapsulation.[268] Other authors revealed that Z. *multiflora* essential oil encapsulated into nanoliposomes can have a higher antibacterial effect in comparison with the free form of the plant's essential oil.[269] Garg *et al*. reported on the pronounced beneficial effects of curcumin in

hamster buccal pouch cancer – it decreased cell proliferation and modulated various cellular responses during tumorigenesis – but pointed out its poor absorption in *in vivo* studies.[73] Further, some other researchers encapsulated the bioactive compounds of *Curcumin longa* – curcuminoids – into nanoparticles and found their significant antioxidant and cytotoxic effects, as the encapsulated curcuminoids acted on the cholinergic and endogenous antioxidant systems.[270] The authors concluded that encapsulation improved the activity of curcuminoids in aqueous medium, in contrast to their original form, which could be explained by the improved water affinity and the reduced size of the nanoparticles. Another study focusing on silymarin demonstrated that the development of a buccal liposomal delivery system allowed an increase in drug penetration and bioavailability of silymarin in comparison with the free silymarin powder.[271]

Thus, the encapsulation technology allows the development of novel delivery systems that ensure the stability and efficiency of natural compounds, as well as their delivery to the target site. The advancements in this technology will increase the efficiency and bioavailability of active agents, but also can widen the range of applications for the encapsulated products, opening new possibilities to develop a new generation of goods.

Table 3
Middle East medicinal plants reported in micro/nanoencapsulation studies

Medicinal plant	Core compound	Method	Encapsulating agent	Brief explanation	Ref.
Punica grantum	Polyphenols and anthocyanin	Spray drying	Maltodextrin Soybean protein isolate	Inlet temperature: 140-160 ± 5 for MD and 100-140 ± 5 for SPI, flow rate: 600 Lh^{-1}, 10 $mLmin^{-1}$ Atomization pressure: 20 psi	333
	Nodal segments of pomegranate	Coaservation	Sodium alginate	----------	334
Satureja khuzistanica	Essential oil	Emulsification	Chitosan	Emulsion in water with Tween 80	335
	Total extract	Solution (emulsion)	Hydrogel alginate	Dried with NaCl	336
Satureja rechingeri	----------	----------	----------	----------	.
Crocus sativus	Anthocyanin	Freeze drying	Arabic gum and maltodextrin	Freeze drying conditions: (-86 °C, Operan-Korea) at 5 mmHg pressure for 42 h; Porous solid materials were crashed in a pestle and mortar, and passed through 25 Mesh sieve and immediately transferred into brown glass containers with screwed caps, then stored in a freezer (-18 °C)	337
	Crocins and picrocrocin	Nanospray drying	Maltodextrin with dextrose	Keep away from direct light and the feed solution was kept in an ice bath. Nozzles with 4.0μm and 7.0μm spray mesh were used.	267
	Crocins	Suspension	Maltosyl-b-cyclodextrin	----------	338
	Crocin	Solution	Maltosyl-b-cyclodextrin	----------	339
	Saffron extracts	Spray drying	Maltodextrin, Arabic gum and gelatin	Inlet and outlet air temperature: at 180 ± 5 °C and 90 ± 5 °C, respectively. The air flow, rate of feeding and atomization pressure: 600 l/h, 5 ml/min and 20 psi, respectively	268
Zataria multiflora	Essential oil	Oil-in-water emulsion and ionic gelation	Chitosan	Various contents of carvacrol, *i.e*., 0, 0.12, 0.24, 0.36, 0.48 and 0.60 g, used to obtain different weight ratios of chitosan to carvacrol of 1:0, 1:0.25, 1:0.50, 1:0.75, 1:1.00 and 1:1.25, respectively. TPP solution (0.5% w/v, 40 mL) was slowly dropped into an o/w emulsion while stirring; agitation was continuously done for 30 min. The final pH of mixture solution was ~5.0. The particles were collected by centrifugation at 10,000 rpm for 10 min at 25 °C	340, 341
	Essential oil	Ionic gelation (CSNP)	Chitosan	pH: 5.6 with NaOH	342
	Essential oil	Nanoliposomes	Soybean phosphatidyl	The lipid film was hydrated with phosphate buffer saline (PBS); (pH 5-7.4)	269

			choline and cholesterol		
	Total phenolic compound	Liposome	Soy bean lecithin (consisting of primary phosphatidyl choline, phosphatidyl ethanolamine and phosphatidyl inositol)	----------	341, 343
Froriepia subpinnata	----------	----------	----------	----------	
Hyssopus officinalis	----------	----------	----------	----------	
Curcuma longa	Curcumin	Solid lipid nanoparticles SLN	Lecithin (phosphatidyl choline), Tween 80	----------	344
	Curcuminoids	Solid dispersion	Polyvinyl pyrrolidone	----------	270, 344
	Total extract	Water in Oil Emulsion	Sodium alginate and carboxymethyl cellulose	pH: 5.6	345
	Curcumin	Solid lipid-based self-emulsifying using spray drying	Aerosol 200 as solid carrier, Lauroglycol FCC, Labrasol and Transcutol HP as oil phase	----------	346
	Curcumin pigments	Spray drying	Edible gelatin and starch	Flow rate of microencapsulating composition, Wff, 60, 70 and 80 mL/min; inlet gas temperature, Tgi 180, 190, and 200 °C; drying air flow; 50, 60 and 70m 3/h. Samples of the spray-dried particles were collected during the experiments	347
	Curcumin	Solid dispersion obtained by spray drying	PVP	----------	348
Ferula assa-foetida		Oil in water emulsion (traditional)		----------	349
Datura stramonium	----------	----------	----------	----------	
Fraxinus excelsior	Total extract	Spray drying	Arabic gum	----------	350
	Embryos	Solution (Ms medium)	Sodium alginate and Sucrose	----------	351
Ficus carica	Embryos	Solution (Ms medium)	Sodium alginate	----------	352
	Embryos	Ms medium	Sodium alginate	----------	353
Artemisia absinthium	Essential oil	Nano cochleates	Soy lecithin	----------	354
Nigella sativa	Essential oil	Spray drying	Maltodextrin DE10	----------	355
	Hexane extract	Spray drying	Arabic gum and maltodextrin	----------	356
	Thymoquinone	Liposome	DPPC	----------	357
Cuminum cyminum	Essential oil (caffeic acid)	Nano gel (self-aggregation)	Chitosan and potato dextrose agar and potato dextrose broth	----------	146
	Cumin oleoresin	Spray drying	Arabic gum, maltodextrin, modified starch	----------	358
	Essential oil	Nano gel (self-assembly)	MA-chitosan	----------	359
Artemisia absinthium	Nodal segments	MS medium	Sodium alginate	----------	360

	Glycyrrhiza uralensis polysaccharide	liposome	Soybean phospholipid	----------	361
	Glycyrrhizic acid	Ionic complexation/ freeze-dried	Chitosan-katira gum	----------	362
Dracocephalum moldavica	Total flavonoids extract	liposome	Soybean phospholipid	----------	363
	Total phenol	Liposome	Phospholipid	----------	160
	Tilianin	Liposome	Phosphatidyl choline	----------	364
Arctium lappa	Polysaccharides	liposome	Soyabean lecithin	----------	365
	Chlorogenic acid and caffeic acid	liposome	Lecithin	----------	366
Citrus aurantium	Total extract (shoot tips)	Solution	Sodium alginate	----------	367
	Flavonoids	Spray drying	Cellulose acetate phthalate	----------	368
	Oil extracts	Nanoemulsion	Different emulsifiers	----------	369
Citrus aurantifolia	Total extract	Liposomes	Soybean phospholipids, triglycerides, and fatty acids	----------	370
Myrtus communis	leaves	Liposome	Egg phosphatidylcholine and cholesterol	Phosphate buffer saline solution (PBS) (pH 7.4)	371
Lawsonia inermis (henna)	Total extract	Spray drying	Potassium bromide.	Henna extract was spray dried using a co-current spray drier apparatus (capacity of the spray drier: 500 mL/h water evaporation).	372
	Total extract	Noisome (thin film hydration method)	Cholesterol and Lawsone	Solvent was evaporated at 60 °C under vacuum in a rotary evaporator. The resulted thin lipid was hydrated with 10 mL of deionized water at 60 °C. The resulting solution was further sonicated in an ultrasonic bath for 30 min at 50 °C. Niosome purification was performed by a 0.22 um membrane.	373
Ziziphus jujube	Protein hydrolysate extracted	Solution	Sodium alginate	----------	374
Ziziphus spina-christi	----------	----------	----------	----------	
Pimpinella Anisum	Essential oil	Freeze drying	Chitosan	----------	375
	Extract/essential oil	Liposome	Phosphatidyl choline	----------	376
Artemisia dracunculus	Essential oil	Nano-emulsion	Oil and surfactant	----------	377
Silybum marianum	Silymarin	liposomes	Lecithin soya powder and cholesterol		378
	Silymarin	liposome	Lecithin and cholesterol		271
Echium amoenum	Total extract	Suspension	Paraffin and erythrocyte	----------	379
	Total extract	Spray drying	----------	----------	380
Malva sylvestris	----------	----------	----------	----------	
Boswellia serrata	Total extract	Phytosome	Lecithin, Phospholipon 90G, cholesterol	----------	381

CONCLUSION

In this review, the most relevant medicinal plants known in the Middle East for their therapeutic properties are presented. These medicinal plants have been used for centuries in the human diet, some as food, others as spices,

aromatic plants, and as medicines. The review summed up their bioactive compounds and biological activities, as well as their traditional uses and known health benefits.

As some of the active components of these plants are very sensitive and are easily degraded during food processing or storage, their encapsulation can be a feasible solution to overcome these limitations. In the last few decades, a significant body of research has yielded various encapsulation systems produced by numerous different methods, such as anti-solvent precipitation, complex coacervation, electrospinning or electrospraying, emulsification, extrusion, fluid bed coating, freeze drying, liposome/nanoliposome, layer-by-layer deposition, phytosome/nanophytosome, solid dispersion, spray drying, sol-gel, suspension cross-linking, freeze spray drying, solid lipid nanoparticle (SLN), nanostructured lipid carriers (NLC), inclusion complexation, thermal gelation and ionic gelation *etc*., which have the potential to be used in several food, pharmaceutical and biological applications.

ACKNOWLEDGMENTS: This work was financially supported by: Base Funding – UIDB/00511/2020 of the Laboratory for Process Engineering, Environment, Biotechnology and Energy – LEPABE – funded by national funds through FCT/MCTES (PIDDAC); Project POCI-01-0145-FEDER-028715 (MicroDelivery – Development of controlled delivery functional systems by microencapsulation of natural and active compounds with therapeutic, nutritional and technological interest), funded by FEDER funds through COMPETE2020 – Programa Operacional Competitividade e Internacionalização (POCI) and by national funds (PIDDAC) through FCT/MCTES; Project "LEPABE-2-ECO-INNOVATION" – NORTE-01-0145-FEDER-000005, funded by Norte Portugal Regional Operational Programme (NORTE 2020), under PORTUGAL 2020 Partnership Agreement, through the European Regional Development Fund (ERDF). Also, Berta Estevinho acknowledges FCT for the contract based on the "Lei do Emprego Científico" (DL 57/2016).

REFERENCES

[1] J. K. Patra, G. Das, S. Lee, S. S. Kang and H. S. Shin, *Trends Food Sci. Technol.*, **82**, 89 (2018), https://doi.org/10.1016/j.tifs.2018.10.001

[2] T. Belwal, S. M. Ezzat, L. Rastrelli, I. D. Bhatt, M. Daglia *et al.*, *Trends Anal. Chem.*, **100**, 82 (2018), https://doi.org/10.1016/j.trac.2017.12.018

[3] S. I. Cameron, R. F. Smith and K. E. Kierstead, *Pharm. Biol.*, **43**, 425 (2008), https://doi.org/10.1080/13880200590963736

[4] A. Hosseini and H. Hosseinzadeh, *Biomed. Pharmacother.*, **99**, 411 (2018), https://doi.org/10.1016/j.biopha.2018.01.072

[5] M. Reza, A. Anaeigoudari and M. Hashemzehi, *J. Tradit. Chinese Med. Sci.*, **9**, 98 (2018), https://doi.org/10.1016/j.jtcme.2018.01.002

[6] Y.-Y. Chan, C.-H. Li, Y.-C. Shen and T.-S. Wu, *Chem. Pharm. Bull. (Tokyo)*, **58**, 61 (2010), https://doi.org/10.1248/cpb.58.61

[7] M. H. Abd El-Razek, S. Ohta, A. A. Ahmed and T. Hirata, *Phytochemistry*, **58**, 1289 (2001), https://doi.org/10.1016/S0031-9422(01)00324-7

[8] V. Sharma, R. C. Agrawal and S. Pandey, *J. Environ. Res. Dev.*, **7**, 1552 (2013)

[9] M. C. Braga, E. C. Silvério Vieira and T. Ferreira de Oliveira, *Food Chem.*, **265**, 308 (2018), https://doi.org/10.1016/j.foodchem.2018.05.096

[10] S. M. Jadouali, H. Atifi, R. Mamouni, K. Majourhat, Z. Bouzouba *et al.*, *J. Saudi Soc. Agric. Sci.*, **18**, 476 (2018), https://doi.org/10.1016/j.jssas.2018.03.007

[11] Z. Khorasanchi, M. Shafiee, F. Kermanshahi, M. Khazaei, M. Ryzhikov *et al.*, *Phytomedicine*, **43**, 21 (2018), https://doi.org/10.1016/j.phymed.2018.03.041

[12] L. Barros, A. M. Carvalho and I. C. F. R. Ferreira, *Food Chem. Toxicol.*, **48**, 1466 (2010), https://doi.org/10.1016/j.fct.2010.03.012

[13] Z. Shah, S. Shafi and J. Magrey, *J. Pharm. Res.*, **12**, 857 (2018)

[14] R. Badoni, D. Kumar, S. Combrinck, C. Cartwright-Jones and A. Viljoen, *J. Ethnopharmacol.*, **155**, 80 (2014)

[15] S. Alinian, J. Razmjoo and H. Zeinali, *Ind. Crop. Prod.*, **81**, 49 (2016), https://doi.org/10.1016/j.indcrop.2015.11.040

[16] V. Aleksic and P. Knezevic, *Microbiol. Res.*, **169**, 240 (2014), https://doi.org/10.1016/j.micres.2013.10.003

[17] A. E. Al-Snafi, *IOSR J. Pharm.*, **6**, 2250 (2016), www.iosrphr.org

[18] M. Reza, A. Anaeigoudari and M. Hashemzehi, *J. Tradit. Chinese Med. Sci.*, **9**, 98 (2018), https://doi.org/10.1016/j.jtcme.2018.01.002

[19] P. R. Bhandari, *J. Tradit. Chinese Med. Sci.*, **5**, 1 (2015), https://doi.org/10.1016/j.jtcme.2014.10.009

[20] B. Saadali, D. Boriky, M. Blaghen, M. Vanhaelen and M. Talbi, *Phytochemistry*, **58**, 1083 (2001)

[21] B. Benítez, M. March-Salas, A. Villa-Kamel, U. Cháves-Jiménez, J. Hernández *et al.*, *J. Ethnopharmacol.*, **219**, 133 (2018), https://doi.org/http://dx.doi.org/10.1016/j.jep.2018.03.007

[22] A. Borah, M. Paw, R. Gogoi, R. Loying, N. Sarma

et al., *Ind. Crop. Prod*., **129**, 448 (2019), https://doi.org/10.1016/j.indcrop.2018.12.035
[23] R. Badoni Semwal, D. K. Semwal, S. Combrinck, C. Cartwright-Jones and A. Viljoen, *J. Ethnopharmacol*., **155**, 80 (2014), https://doi.org/10.1016/j.jep.2014.05.042
[24] F. Zhao, L. Wang and K. Liu, *J. Ethnopharmacol*., **122**, 457 (2009), https://doi.org/10.1016/j.jep.2009.01.038
[25] Q. H. Gao, C. Sen Wu and M. Wang, *J. Agric. Food Chem*., **61**, 3351 (2013), https://doi.org/10.1021/jf4007032
[26] Z. Mazarei and H. Rafati, *LWT*, **100**, 328 (2019), https://doi.org/10.1016/j.lwt.2018.10.094
[27] S. M. Hasheminya, R. R. Mokarram, B. Ghanbarzadeh, H. Hamishekar, H. S. Kafil *et al*., *Polym. Test*., **73**, 377 (2019), https://doi.org/10.1016/j.polymertesting.2018.12.002
[28] S. Siavash Saei-Dehkordi, A. A. Fallah, M. Heidari-Nasirabadi and M. Moradi, *Int. J. Food Sci. Technol*., **47**, 1579 (2012), https://doi.org/10.1111/j.1365-2621.2012.03006.x
[29] F. Jafari, F. Ghavidel and M. M. Zarshenas, *J. Acupunct. Meridian Stud*., **9**, 118 (2016), https://doi.org/10.1016/j.jams.2016.04.003
[30] E. Giannouli, D. Athanasopoulos, G. Panagopoulos, S. Tsiara and C. E. Karageorgiou, *J. Neurol. Sci*., **333**, e703 (2013), https://doi.org/10.1016/j.jns.2013.07.2427
[31] E. Kakouri, D. Daferera, S. Paramithiotis, K. Astraka, E. H. Drosinos *et al*., *J. Dermatol. Sci*., **4**, 66 (2017), https://doi.org/10.1016/j.jarmap.2016.09.002
[32] T. C. Delozier, G. E. Kissling, S. J. Coulter, D. Dai, J. F. Foley *et al*., *Signal Transduct*., **35**, 682 (2009), https://doi.org/10.1124/dmd.106.012823.Detection
[33] S. I. Bukhari, M. Manzoor and M. K. Dhar, *Biomed. Pharmacother*., **98**, 733 (2018), https://doi.org/10.1016/J.BIOPHA.2017.12.090
[34] K. Bajbouj, J. Schulze-Luehrmann, S. Diermeier, A. Amin and R. Schneider-Stock, *BMC Complement. Altern. Med*., **12** (2012), https://doi.org/10.1186/1472-6882-12-69
[35] E. Kakouri, D. Daferera, S. Paramithiotis, K. Astraka, E. H. Drosinos *et al*., *J. Dermatol. Sci*., **4**, 66 (2017), https://doi.org/10.1016/j.jarmap.2016.09.002
[36] M. H. Boskabady and L. Gholami Mahtaj, *BMC Complement. Altern. Med*., **15**, 1 (2015), https://doi.org/10.1186/s12906-015-0574-y
[37] F. Akrami, A. Rodríguez-Lafuente, K. Bentayeb, D. Pezo, S. R. Ghalebi *et al*., *LWT - Food Sci. Technol*., **60**, 929 (2015), https://doi.org/10.1016/j.lwt.2014.09.051
[38] M. Mahboubi, *J. Integr. Med*., **16**, 20 (2018), https://doi.org/10.1016/j.joim.2017.12.006
[39] M. R. Khazdair, V. Ghorani, A. Alavinezhad and M. H. Boskabady, *Fundam. Clin. Pharmacol*., **32**, 26 (2018), https://doi.org/10.1111/fcp.12331
[40] M. Moradi, H. Tajik, S. Mehdi, R. Rohani and A. Mahmoudian, *LWT - Food Sci. Technol*., **72**, 37 (2016), https://doi.org/10.1016/j.lwt.2016.04.026
[41] A. Mansour, K. Enayat, M. S. Neda and A. Behzad, *Asian Pac. J. Trop. Med*., **3**, 439 (2010), https://doi.org/10.1016/S1995-7645(10)60105-8
[42] M. Shokrzadeh, M. Azadbakht, N. Ahangar, H. Naderi and S. Saeedi Saravi, *Pharmacogn. Mag*., **6**, 102 (2010), https://doi.org/10.4103/0973-1296.62894
[43] M. H. Boskabady, M. Kaveh, N. Eftekhar and A. Nemati, *Evidence-based Complement. Altern. Med*., **2011** (2011), https://doi.org/10.1155/2011/857124
[44] F. V. Silva, A. G. Guimarães, E. R. S. Silva, B. P. Sousa-Neto, F. D. F. Machado *et al*., *J. Med. Food*., **15**, 984 (2012), https://doi.org/10.1089/jmf.2012.0102
[45] M. H. Boskabady and L. Gholami Mhtaj, *Biomed. Res. Int*., **2014** (2014), https://doi.org/10.1155/2014/802189
[46] M. Jenkins, *Acupunct. Med*., **11**, 106 (1993), https://doi.org/10.1136/aim.11.2.106-a
[47] M. A. Maggiore, A. A. Albanese, L. B. Gende, M. J. Eguaras, G. M. Denegri *et al*., *Parasitol. Res*., **110**, 1103 (2012), https://doi.org/10.1007/s00436-011-2595-x
[48] M. Moazeni, H. Borji, M. Saboor Darbandi and M. J. Saharkhiz, *Res. Vet. Sci*., **114**, 308 (2017), https://doi.org/10.1016/j.rvsc.2017.06.003
[49] H. Sajed, A. Sahebkar and M. Iranshahi, *J. Ethnopharmacol*., **145**, 686 (2013), https://doi.org/10.1016/j.jep.2012.12.018
[50] M. Ramezani, H. Hosseinzadeh and S. Samizadeh, *J. Ethnopharmacol*., **91**, 167 (2004), https://doi.org/10.1016/j.jep.2003.12.016
[51] A. Naeini, A. R. Khosravi, M. Chitsaz, H. Shokri and M. Kamlnegad, *J. Mycol. Med*., **22**, 211 (2012), https://doi.org/10.1016/j.mycmed.2012.04.006
[52] M. K. Kaleji and M. R. Ardakani, *Iran. J. Plant Physiol*., 2457 (2018), https://doi.org/10.22034/ijpp.2018.540990
[53] C. Yang, S. Chhabra, J.-Y. Hong and Th. J. Smith, *J. Nutr*., **131**, 951 (2001), https://doi.org/10.1093/jn/131.3.1041S
[54] C. A. Jaleel, P. Manivannan, B. Sankar, A. Kishorekumar, R. Gopi *et al*., *Colloid. Surfaces B Biointerfaces*, **60**, 7 (2007), https://doi.org/10.1016/j.colsurfb.2007.05.012
[55] V. Pandey, R. S. Verma, A. Chauhan and R. Tiwari, *J. Herb. Med*., **4**, 89 (2014), https://doi.org/10.1016/j.hermed.2013.12.001
[56] I. Bajalan, R. Rouzbahani, A. G. Pirbalouti and F. Maggi, *Ind. Crop. Prod*., **107**, 305 (2017), https://doi.org/10.1016/j.indcrop.2017.05.063
[57] H. Matsuura, H. Miyazaki, C. Asakawa, M. Amano, T. Yoshihara *et al*., *Phytochemistry*, **65**, 91 (2004), https://doi.org/10.1016/j.phytochem.2003.10.009
[58] E. T. Rfsse and F. W. Parrish, *Carbohyd. Res*., **18**, 381 (1971)
[59] A. M. Džamíc, M. D. Sokovíc, M. Novakovíc, M. Jadranin, M. S. Ristíc *et al*., *Ind. Crop. Prod*., **51**, 401 (2013), https://doi.org/10.1016/j.indcrop.2013.09.038

[60] G. Hatipo, M. Sökmen, E. Bektas, D. Daferera and A. Sökmen, *Ind. Crop. Prod.*, **43**, 427 (2013), https://doi.org/10.1016/j.indcrop.2012.07.028
[61] W. Kreis, M. H. Kaplan, J. Freeman, D. K. Sun and P. S. Sarin, *Antiviral Res.*, **14**, 323 (1990), https://doi.org/10.1016/0166-3542(90)90051-8
[62] M. P. Letessier, K. P. Svoboda and D. R. Walters, *J. Phytopathol.*, **149**, 673 (2001), https://doi.org/10.1046/j.1439-0434.2001.00692.x
[63] L. Nedorostova, P. Kloucek, L. Kokoska, M. Stolcova and J. Pulkrabek, *Food Control*, **20**, 157 (2009), https://doi.org/10.1016/j.foodcont.2008.03.007
[64] Z. Váradyová, J. Pisarčíková, M. Babják, A. Hodges, D. Mravčáková *et al.*, *Exp. Parasitol.*, **195**, 71 (2018), https://doi.org/10.1016/j.exppara.2018.10.009
[65] M. Mahboubi, G. Haghi and N. Kazempour, *J. Biol. Act. Prod. From Nat.*, **1**, 132 (2011), https://doi.org/10.1080/22311866.2011.10719080
[66] H. Özer, M. Sökmen, A. Adigüzel, H. Kiliç, F. Şahin *et al.*, *Ital. J. Food Sci.*, **18**, 73 (2006)
[67] C. Araújo and L. Leon, *Mem. Inst. Oswaldo Cruz.*, **96**, 723 (2001), https://doi.org/10.1590/S0074-02762001000500026
[68] B. Salehi, Z. Stojanovi-Radic, J. Matejic, M. Sharfi-Radi, N. V. Anil Kumar *et al.*, *Eur. J. Med. Chem.*, **163**, 527 (2019)
[69] A. Sahebkar, *Integr. Cancer Ther.*, **15**, 333 (2016), https://doi.org/10.1177/1534735415624139
[70] M. C. Braga, E. C. Silvério Vieira and T. Ferreira de Oliveira, *Food Chem.*, **265**, 308 (2018), https://doi.org/10.1016/j.foodchem.2018.05.096
[71] T. Ak and I. Gülçin, *Chem. Biol. Interact.*, **174**, 27 (2008), https://doi.org/10.1016/j.cbi.2008.05.003
[72] I. Ragunathan and N. Panneerselvam, *J. Zhejiang Univ. Sci. B.*, **8**, 470 (2007), https://doi.org/10.1631/jzus.2007.B0470
[73] R. Garg, A. Ingle and G. Maru, *Toxicol. Appl. Pharmacol.*, **232**, 428 (2008), https://doi.org/10.1016/j.taap.2008.07.007
[74] W. Zhu and P. C. W. Fung, *Free Radic. Biol. Med.*, **29**, 870 (2000), https://doi.org/10.1016/S0891-5849(00)00396-8
[75] I. Dib and F. E. El Alaoui-Faris, *Biomed. Pharmacother.*, **109**, 1884 (2019), https://doi.org/10.1016/j.biopha.2018.10.149
[76] F. Yang, G. P. Lim, A. N. Begum, O. J. Ubeda, M. R. Simmons *et al.*, *J. Biol. Chem.*, **280**, 5892 (2005), https://doi.org/10.1074/jbc.M404751200
[77] I. Mohanty, D. S. Arya and S. K. Gupta, *BMC Complement. Altern. Med.*, **6**, 1 (2006), https://doi.org/10.1186/1472-6882-6-3
[78] S. Rahmani, S. Asgary, G. Askari, M. Keshvari, M. Hatamipour *et al.*, *Phytother. Res.*, **30**, 1540 (2016), https://doi.org/10.1002/ptr.5659
[79] J. L. Funk, J. B. Frye, J. N. Oyarzo, N. Kuscuoglu, J. Wilson *et al.*, *Arthritis Rheum.*, **54**, 3452 (2006), https://doi.org/10.1002/art.22180
[80] S. K. Kulkarni, K. K. Akula and J. Deshpande, *Pharmacology*, **89**, 83 (2012), https://doi.org/10.1159/000335660
[81] S. Khattak, Saeed-ur-Rehman, H. U. Shah, W. Ahmad and M. Ahmad, *Fitoterapia*, **76**, 254 (2005), https://doi.org/10.1016/j.fitote.2004.12.012
[82] D. Saitawee, A. Teerakapong, N. P. Morales, P. Jitprasertwong and D. Hormdee, *Photodiagnosis Photodyn. Ther.*, **22**, 101 (2018), https://doi.org/10.1016/j.pdpdt.2018.03.001
[83] T. Farkhondeh and S. Samarghandian, *Cardiovasc. Hematol. Disord. Drug Targets*, **16**, 30 (2016), https://doi.org/10.2174/1871529X16666160802144510
[84] T. Farkhondeh, S. Samarghandian and F. Samini, *Asian Pac. J. Trop. Med.*, **9**, 947 (2016), https://doi.org/10.1016/j.apjtm.2016.07.027
[85] G. Kavoosi and V. Rowshan, *Food Chem.*, **138**, 2180 (2013), https://doi.org/10.1016/j.foodchem.2012.11.131
[86] F. Syed, R. Taj, N. Shaheen, M. Norin and S. Khan, *African J. Pharm. Pharmacol.*, **8**, 100 (2014), https://doi.org/10.5897/AJPP2013.3971
[87] Z. Boghrati and M. Iranshahi, *J. Herb. Med.*, **16**, 100244 (2019), https://doi.org/10.1016/j.hermed.2018.10.009
[88] A. Goudah, K. Abo-El-Sooud and M. A. Yousef, *Vet. World.*, **8**, 584 (2015), https://doi.org/10.14202/vetworld.2015.584-589.
[89] M. Iranshahy, *J. Ethnopharmacol.*, **134**, 1 (2011), https://doi.org/10.1016/j.jep.2010.11.067
[90] K. Zomorodian, J. Saharkhiz, K. Pakshir, Z. Immeripour and A. Sadatsharifi, *Biocatal. Agric. Biotechnol.*, **14**, 300 (2018), https://doi.org/10.1016/j.bcab.2018.03.014
[91] N. Boke, F. Musyoka, M. Saidi, N. Dudai and N. Bernstein, *J. Dermatol. Sci.*, **2**, 21 (2015), https://doi.org/10.1016/j.jarmap.2015.01.003
[92] E. Latifi, A. A. Mohammadpour and B. F. H. Nourani, *Biomed. Pharmacother.*, **110**, 197 (2019), https://doi.org/10.1016/j.biopha.2018.10.152
[93] S. Majid, A. Abdian-Asl and M. Taheri, *J. Ayurveda Integr. Med.*, **8**, (2017), https://doi.org/10.1016/j.jaim.2017.02.013
[94] S. Bahramikia and R. Yazdanparast, *Phyther. Res.*, **26**, 1581 (2012), https://doi.org/10.1002/ptr.4617
[95] P. Soni, A. A. Siddiqui, J. Dwivedi and V. Soni, *Asian Pac. J. Trop. Biomed.*, **2**, 1002 (2012), https://doi.org/10.1016/S2221-1691(13)60014-3
[96] B. Y. Yang, Y. G. Xia, Y. Liu, L. Li, H. Jiang *et al.*, *Phytochem. Lett.*, **8**, 92 (2014), https://doi.org/10.1016/j.phytol.2014.02.008
[97] M. T. Gutierrez-Lugo, T. Barrientos-Benítez, B. Luna, R. M. Ramirez-Gama, R. Bye *et al.*, *Phytomedicine*, **2**, 341 (1996), https://doi.org/10.1016/S0944-7113(96)80079-1
[98] Z. Saddiqe, U. Wahab, A. Maimoona, R. Raheel and M. Iram, *South African J. Bot.*, **117**, 282 (2018), https://doi.org/10.1016/j.sajb.2018.05.031
[99] D. Diker, D. Markovitz, M. Rothman and U. Sendovski, *Eur. J. Intern. Med.*, **18**, 336 (2007), https://doi.org/10.1016/j.ejim.2006.09.035

[100] S. Bahadur, M. S. Khan, M. Shah, M. Shuaib, M. Ahmad *et al*., *Acta Ecol. Sin*., **40**, 1 (2018), https://doi.org/10.1016/j.chnaes.2018.12.006
[101] P. Deepa, K. Sowndhararajan, S. Kim and S. J. Park, *J. Ethnopharmacol*., **215**, 210 (2018), https://doi.org/10.1016/j.jep.2017.12.045
[102] K. C. Chinsembu, *J. Herb. Med*., **15**, 100230 (2019), https://doi.org/10.1016/j.hermed.2018.09.001
[103] S. Abbasi, M. Kamalinejad, D. Babaie, S. M. Shams, Z. Sadr *et al*., *Complement. Ther. Med*., **35**, 85 (2017), https://doi.org/10.1016/j.ctim.2017.10.003
[104] Z. Nemati, F. R. Blattner, H. Kerndorff, O. Erol and D. Harpke, *Mol. Phylogenet. Evol*., **127**, 891 (2018), https://doi.org/10.1016/j.ympev.2018.06.036
[105] P. A. Davis and C. K. Iwahashi, *Cancer Lett*., **165**, 27 (2001), https://doi.org/10.1016/S0304-3835(01)00425-6
[106] M. S. Motaharifard, Z. Jafari, M. S. Paknejad, L. Oveidzadeh and M. Karimi, *J. Integr. Med*., **14**, 429 (2016), https://doi.org/10.1016/S2095-4964(16)60278-9
[107] M. Shukranul, H. Khairana and J. Ibrahim, *Evidence-Based Complement. Altern. Med*., **2013**, 974256 (2013), https://doi.org/10.1155/2013/974256
[108] M. A. A. Rashid, K. Ibrahim and N. Mohammd Mahdi, *J. Babylon Univ. Appl. Sci*., **22**, 1620 (2014)
[109] S. M. F. Bessada, J. C. M. Barreira and M. B. P. P. Oliveira, *Ind. Crop. Prod*., **76**, 604 (2015), https://doi.org/10.1016/j.indcrop.2015.07.073
[110] H. T. Nguyen and Z. É. Németh, *J. Appl. Res. Med. Aromat. Plants*, **3**, 143 (2016), https://doi.org/10.1016/j.jarmap.2016.07.005
[111] S. Dehdari, H. Hajimehdipoor, S. Esmaeili, R. Choopani and S. A. Mortazavi, *J. Integr. Med*., **16**, 90 (2018), https://doi.org/10.1016/j.joim.2018.01.002
[112] M. Mojarrab, M. S. Lagzian, S. A. Emami, J. Asili and Z. Tayarani-Najaran, *Brazilian J. Pharmacogn*., **23**, 783 (2013), https://doi.org/10.1590/S0102-695X2013000500010
[113] A. Rustaiyan and S. Masoudi, *Phytochem. Lett*., **4**, 440 (2011), https://doi.org/10.1016/j.phytol.2011.07.003
[114] K. Morteza-Semnani and M. Akbarzadeh, *J. Essent. Oil Res*., **17**, 321 (2005), https://doi.org/10.1080/10412905.2005.9698918
[115] A. C. de Souza Chagas, C. S. Georgetti, C. O. de Carvalho, M. C. de Sena Oliveira, R. A. Rodrigues *et al*., *Rev. Bras. Parasitol. Vet*., **20**, 31 (2011), https://doi.org/10.1590/S1984-29612011000100007
[116] M. Ali, B. H. Abbasi and G. S. Ali, *Plant Cell. Tissue Organ Cult*., **120**, 1099 (2015), https://doi.org/10.1007/s11240-014-0666-2
[117] M. Bailen, L. F. Julio, C. E. Diaz, J. Sanz, R. A. Martínez-Díaz *et al*., *Ind. Crop. Prod*., **49**, 102 (2013), https://doi.org/10.1016/j.indcrop.2013.04.055
[118] J. M. Canadanovic-Brunet, S. M. Djilas, G. S. Cetkovic and V. T. Tumbas, *J. Sci. Food Agric*., **85**, 265 (2005), https://doi.org/10.1002/jsfa.1950
[119] R. Onbas, A. Kazan, A. Nalbantsoy and O. Yesil-Celiktas, *Plant Foods Hum. Nutr*., **71**, 286 (2016), https://doi.org/10.1007/s11130-016-0558-1
[120] P. M. Shafi, G. M. K. Nambiar, R. A. Clery, Y. R. Sarma and S. S. Veena, *J. Essent. Oil Res*., **16**, 377 (2004), https://doi.org/10.1080/10412905.2004.9698748
[121] R. Tzenkova, Z. Kamenarska, A. Draganov and A. Atanassov, *Biotechnol. Biotechnol. Equip*., **24**, 1833 (2010), https://doi.org/10.2478/V10133-010-0030-6
[122] M. Haddad, S. Zein, H. Shahrour, K. Hamadeh, N. Karaki and H. Kanaan, *Asian Pac. J. Trop. Biomed*., **7**, 157 (2017), https://doi.org/10.1016/j.apjtb.2016.11.024
[123] P. A. Sofi, N. A. Zeerak and P. Singh, *Turk. J. Biol*., **33**, 249 (2009), https://doi.org/10.3906/biy-0803-18
[124] M. Mendel, M. Chłopecka, N. Dziekan and W. Karlik, *Anim. Feed Sci. Technol*., **230**, 30 (2017), https://doi.org/10.1016/j.anifeedsci.2017.05.008
[125] H. Hassanzadazar, B. Taami, M. Aminzare and S. Daneshamooz, *J. Appl. Pharm. Sci*., **8**, 150 (2018), https://doi.org/10.7324/JAPS.2018.81019
[126] T. Ali, K. Saeed, M. Abdullah and I. Murtaza, *Osong Public Heal. Res. Perspect*., **5**, 358 (2014), https://doi.org/10.1016/j.phrp.2014.11.005
[127] I. Stappen, N. Tabanca, A. Ali, D. E. Wedge, V. Gochev *et al*., *Open Chem*., **16**, 52 (2017), https://doi.org/10.1515/chem-2018-0028
[128] S. Lahlou, A. Tahraoui, Z. Israili and B. Lyoussi, *J. Ethnopharmacol*., **110**, 458 (2007), https://doi.org/10.1016/j.jep.2006.10.005
[129] M. Zendehdel, Z. Torabi and S. Hassanpour, *Vet. Med. (Praha)*, **60**, 63 (2015), https://doi.org/10.17221/7988-VETMED
[130] A. Bogucka-Kocka, H. D. Smolarz and J. Kocki, *Fitoterapia*, **79**, 487 (2008), https://doi.org/10.1016/j.fitote.2008.07.002
[131] F. K. Nasab and A. K. Reza, *J. Ethnopharmacol*., **154**, 190 (2014)
[132] M. A. Fard and A. Shojaii, *BioMed. Res. Int*., **2013**, 692751 (2013), https://doi.org/10.1155/2013/692751
[133] S. S. Hosseini, F. Nadjafi, M. H. Asareh and H. Rezadoost, *Sci. Hortic. (Amsterdam)*, **233**, 1 (2018), https://doi.org/10.1016/j.scienta.2018.01.038
[134] S. Gharby, H. Harhar, D. Guillaume, A. Roudani, S. Boulbaroud *et al*., *J. Saudi Soc. Agric. Sci*., **14**, 172 (2015), https://doi.org/10.1016/j.jssas.2013.12.001
[135] C. C. Toma, G. M. Simu, D. Hanganu, N. Olah, F. M. G. Vata *et al*., *Farmacia*, **58**, 458 (2010)
[136] H. Shokri, A. Sharifzadeh and I. Ashrafi Tamai, *J. Mycol. Med*., **22**, 211 (2012), https://doi.org/10.1016/j.mycmed.2012.04.006
[137] W. Kooti, Z. Hasanzadeh-Noohi, N. Sharafi-Ahvazi, M. Asadi-Samani and D. Ashtary-Larky, *Chin. J. Nat. Med*., **14**, 732 (2016), https://doi.org/10.1016/S1875-5364(16)30088-7
[138] S. Darakhshan, A. Bidmeshki Pour, A. Hosseinzadeh Colagar and S. Sisakhtnezhad, *Pharmacol. Res*., **95–96**, 138 (2015), https://doi.org/10.1016/j.phrs.2015.03.011

[139] R. A. Khosravi, H. Shokri, Z. Farahnejat, R. Chalangari and M. Katalin, *Chin. J. Nat. Med.*, **11**, 43 (2013), https://doi.org/10.1016/S1875-5364(13)60006-0
[140] M. L. Mathur, J. Gaur, R. Sharma and K. R. Haldiya, *J. Endocrinol. Metab.*, **1**, 1 (2011), https://doi.org/10.4021/jem12e
[141] J. K. Grover, S. Yadav and V. Vats, *J. Ethnopharmacol.*, **81**, 81 (2002), https://doi.org/10.1016/S0378-8741(02)00059-4
[142] J. Heshmati and N. Namaz, *Complement. Ther. Med.*, **23**, 275 (2015), https://doi.org/10.1016/j.ctim.2015.01.013
[143] A. Rezaei, A. Farzadfard, A. Amirahmadi, M. Alemi and M. Khademi, *J. Ethnopharmacol.*, **175**, 567 (2015), https://doi.org/10.1016/j.jep.2015.08.010
[144] M. Kanter, M. Akpolat and C. Aktas, *J. Mol. Histol.*, **40**, 379 (2009), https://doi.org/10.1007/s10735-009-9251-0
[145] R. Shafiee-Nick, A. Ghorbani, F. Vafaee Bagheri and H. Rakhshandeh, *Adv. Pharmacol. Sci.*, **2012**, 789796 (2012), https://doi.org/10.1155/2012/789796
[146] S. Zhaveh, A. Mohsenifar, M. Beiki, S. T. Khalili and A. Abdollahi *et al.*, *Ind. Crop. Prod.*, **69**, 251 (2015), https://doi.org/10.1016/j.indcrop.2014.01.033
[147] N. S. Iacobellis, P. Lo Cantore, F. Capasso and F. Senatore, *J. Agric. Food Chem.*, **53**, 57 (2005), https://doi.org/10.1021/jf0487351
[148] M. Bahmani, A. Zargaran and M. Rafieian-Kopaei, *Brazilian J. Pharmacogn.*, **24**, 468 (2014), https://doi.org/10.1016/j.bjp.2014.08.001
[149] A. S. Jesuthasan and D. I. Uluwaduge, *J. Integr. Med.*, **15**, 19 (2017), https://doi.org/10.1016/S2095-4964(17)60317-0
[150] M. H. Minooeianhaghighi, L. Sepehrian and H. Shokri, *J. Med. Mycol.*, **27**, 65 (2017), https://doi.org/10.1016/j.mycmed.2016.09.002
[151] A. Shakeri, M. Masullo, G. D'Urso, M. Iranshahi, P. Montoro *et al.*, *Food Chem.*, **248**, 128 (2018), https://doi.org/10.1016/j.foodchem.2017.12.031
[152] M. Ravikumar, P. Sarita, R. G. J. Naga and R. S. Bhuloka, *J. Environ. Res. Dev.*, **7**, 1209 (2013)
[153] Z. Abasian, A. Rostamzadeh, M. Mohammadi, M. Hosseini and M. Rafieian-Kopaei, *Middle East Fertil. Soc. J.*, **23**, 255 (2018), https://doi.org/10.1016/j.mefs.2018.04.005
[154] M. Aalikhani Pour, S. Sardari, A. Eslamifar, M. Rezvani, A. Azhar *et al.*, *J. Herb. Med.*, **6**, 128 (2016), https://doi.org/10.1016/j.hermed.2016.05.002
[155] K. Muthiah and S. Suja, *Transform. Bus. Econ.*, **16**, 85 (2017), https://doi.org/10.1002/ptr
[156] M. Sadat-Hosseini, M. Farajpour, N. Boroomand and F. Solaimani-Sardou, *J. Ethnopharmacol.*, **199**, 194 (2017), https://doi.org/10.1016/j.jep.2017.02.006
[157] M. Bahmani, H. Shirzad, M. Majlesi, N. Shahinfard and M. Rafieian-Kopaei, *Asian Pac. J. Trop. Med.*, **7**, S43 (2014), https://doi.org/10.1016/S1995-7645(14)60202-9
[158] H. Kamali, E. Khodaverdi, F. Hadizadeh and S. H. Ghaziaskar, *J. Supercrit. Fluids*, **107**, 307 (2016), https://doi.org/10.1016/j.supflu.2015.09.028
[159] F. Zamansoltani, M. Nassiri-Asl and R. Karimi, P. Mamaghani-Rad, *Pharmacologyonline*, **438**, 432 (2008), https://pharmacologyonline.silae.it/files/archives/2008/vol1/42_Farzaneh.pdf
[160] K. Dastmalchi, H. J. D. Dorman, M. Kosar and R. Hiltunen, *LWT - Food Sci. Technol.*, **40**, 239 (2007), https://doi.org/10.1016/j.lwt.2005.09.019
[161] M. Frąc, K. Oszust, A. Kocira and S. Kocira, *Agric. Agric. Sci. Procedia*, **7**, 74 (2015), https://doi.org/10.1016/j.aaspro.2015.12.036
[162] J. Carlotto, L. M. de Souza, C. H. Baggio, M. F. de P. Werner, D. Maria-Ferreira *et al.*, *Int. J. Biol. Macromol.*, **91**, 954 (2016), https://doi.org/10.1016/j.ijbiomac.2016.06.033
[163] M. Shareef, M. A. Ashraf and M. Sarfraz, *Saudi Pharm. J.*, **24**, 233 (2016), https://doi.org/10.1016/j.jsps.2016.04.018
[164] M. Gilca, G. S. Tiplica and C. M. Salavastru, *Clin. Dermatol.*, **36**, 338 (2018), https://doi.org/10.1016/j.clindermatol.2018.03.008
[165] L. Possebon, I. de Souza Lima Lebron, L. Furlan da Silva, J. Tagliaferri Paletta, B. G. Glad *et al.*, *Biomed. Pharmacother.*, **99**, 591 (2018), https://doi.org/10.1016/j.biopha.2018.01.106
[166] M. Gentil, J. V. Pereira, Y. T. Corrêa Silva Sousa, R. Pietro, M. D. Sousa Neto *et al.*, *Phyther. Res.*, **20**, 184 (2006), https://doi.org/10.1002/ptr.1829
[167] A. F. El-Kott and M. M. Bin-Meferij, *Curr. Ther. Res. - Clin. Exp.*, **77**, 73 (2015), https://doi.org/10.1016/j.curtheres.2015.05.001
[168] S. C. Lin, C. H. Lin, C. C. Lin, Y. H. Lin, C. F. Chen *et al.*, *J. Biomed. Sci.*, **9**, 401 (2002), https://doi.org/10.1007/BF02256533
[169] W. Liu, J. Wang, Z. Zhang, J. Xu, Z. Xie, *Int. J. Biol. Macromol.*, **65**, 446 (2014), https://doi.org/10.1016/j.ijbiomac.2014.01.062
[170] D. Yi, C. L. Alvim Kamei, T. Cools, S. Vanderauwera, N. Takahashi *et al.*, *Plant Cell.*, **26**, 296 (2014), https://doi.org/10.1105/tpc.113.118943
[171] C. L. Chan, R. Gan, N. P. Shah and H. Corke, *Food Biosci.*, **26**, 185 (2018), https://doi.org/10.1016/j.fbio.2018.10.016
[172] J. A. Khan and S. Hanee, *Int. J. Appl. Biol. Pharm. Technol.*, **2**, 23 (2011)
[173] X. Zhai, C. Zhu, Y. Zhang, J. Sun, A. Alim *et al.*, *Carbohyd. Polym.*, **202**, 461 (2018), https://doi.org/10.1016/j.carbpol.2018.09.013
[174] E. P. Lansky and R. A. Newman, *J. Ethnopharmacol.*, **109**, 177 (2007), https://doi.org/10.1016/j.jep.2006.09.006
[175] N. R. Rathod, D. Biswas, H. R. Chitme, S. Ratna, I. S. Muchandi *et al.*, *J. Ethnopharmacol.*, **140**, 234 (2012), https://doi.org/10.1016/j.jep.2012.01.003
[176] I. Celik, A. Temur and I. Isik, *Food Chem. Toxicol.*, **47**, 145 (2009), https://doi.org/10.1016/j.fct.2008.10.020

[177] F. I. D. Afolayan, O. M. Adegbolagun, B. Irungu, L. Kangethe, J. Orwa *et al*., *J. Ethnopharmacol*., **191**, 188 (2016), https://doi.org/10.1016/j.jep.2016.06.045
[178] K. Dhaouadi, W. Meliti, S. Dallali, M. Belkhir, S. Ouerghemmi *et al*., *Ind. Crop. Prod*., **77**, 544 (2015), https://doi.org/10.1016/j.indcrop.2015.09.037
[179] I. Abulyazid, E. M. E. Mahdy and R. M. Ahmed, *Arab. J. Chem*., **6**, 265 (2013), https://doi.org/10.1016/j.arabjc.2010.10.005
[180] M. Kannahi and T. Nadu, *Int. J. Curr. Microbiol. Appl. Sci*., **2**, 342 (2013)
[181] S. Ahmadian and M. A. A. Fakhree, *Med. Hypotheses*, **73**, 629 (2009), https://doi.org/10.1016/j.mehy.2009.06.001
[182] W. B. Wan Nik, H. M. Hajar, M. J. Suriani, M. G. M. Sabri and M. J. Ghazali, *J. Mech. Eng. Sci*., **11** (2017)
[183] F. Mouhajir, J. B. Hudson, M. Rejdali and G. H. N. Towers, *Pharm. Biol*., **39**, 364 (2001), https://doi.org/10.1076/phbi.39.5.364.5892
[184] K. Sagar and G. M. Vidyasagar, *J. Appl. Pharm. Sci*., **3**, 77 (2013), https://doi.org/10.7324/JAPS.2013.30213
[185] M. Kulshreshtha, M. Goswami, C. V. Rao and S. Yadav, *J. Appl. Pharm. Sci*., **1**, 69 (2011)
[186] J. Sharma, S. Gairola, R. D. Gaur and R. M. Painuli, *J. Ethnopharmacol*., **143**, 262 (2012), https://doi.org/10.1016/j.jep.2012.06.034
[187] K. Chowk and S. Building, *Nat. Prod. Radiance*, **3**, 406 (2004)
[188] K. Biffi, A. G. de Rezende, L. de Almeida, C. K. B. Yajima, F. C. Barbieri *et al*., *Sci. Med. (Porto Alegre)*, **23**, 34 (2013)
[189] A. B. Hsouna, M. Trigui, G. Culioli, Y. Blache and S. Jaoua, *Food Chem*., **125**, 193 (2011), https://doi.org/10.1016/j.foodchem.2010.08.060
[190] European Commission, SCCS/1532/14, 1 (2014), https://doi.org/10.2772/47128
[191] X. Ji, Q. Peng, Y. Yuan, J. Shen, X. Xie *et al*., *Food Chem*., **227**, 349 (2017), https://doi.org/10.1016/j.foodchem.2017.01.074
[192] M. A. Hossain, *J. King Saud Univ. - Sci*., **31**, 1352 (2018), https://doi.org/10.1016/j.jksus.2018.12.003
[193] S. Almansa, F. Hernández, P. Legua, M. Nicolás-Almansa and A. Amorós, *J. Sci. Food Agric*., **96**, 4098 (2016), https://doi.org/10.1002/jsfa.7610
[194] F. A. Al-Bayati, *J. Ethnopharmacol*., **116**, 403 (2008), https://doi.org/10.1016/j.jep.2007.12.003
[195] S. F. Abouzid and A. A. Mohamed, *J. Ethnobiol. Ethnomed*., **7**, 1 (2011), https://doi.org/10.1186/1746-4269-7-18
[196] S. Logendra, D. M. Ribnicky, H. Yang, A. Poulev, J. Ma *et al*., *Phytochemistry*, **67**, 1539 (2006), https://doi.org/10.1016/j.phytochem.2006.05.015
[197] M. Mitoshi, I. Kuriyama, H. Nakayama, H. Miyazato, K. Sugimoto *et al*., *J. Agric. Food Chem*., **60**, 11343 (2012), https://doi.org/10.1021/jf303377f
[198] D. M. Ribnicky, A. Poulev, J. O'Neal, G. Wnorowski, D. E. Malek *et al*., *Food Chem. Toxicol*., **42**, 585 (2004), https://doi.org/10.1016/j.fct.2003.11.002
[199] D. M. Ribnicky, P. Kuhn, A. Poulev, S. Logendra, A. Zuberi *et al*., *Int. J. Pharm*., **370**, 87 (2009), https://doi.org/10.1016/j.ijpharm.2008.11.012
[200] N. S. Ajikumaran, K. Rajani, S. N. Akhila and B. Sabulal, *Phytomedicine*, **50**, 231 (2017), https://doi.org/10.1016/J.PHYMED.2017.08.011
[201] M. Fomani, E. Ngeufa Happi, A. Nouga Bisoue, J. C. Ndom, A. F. Kamdem Waffo *et al*., *Bioorg. Med. Chem. Lett*., **26**, 306 (2016), https://doi.org/10.1016/j.bmcl.2015.12.028
[202] S. Bissim, S. B. Kenmogne, A. T. Tcho, M. Lateef, A. Ahmed *et al*., *Phytochem. Lett*., **29**, 148 (2019), https://doi.org/10.1016/j.phytol.2018.12.010
[203] J. A. S. Suryawanshi, *African J. Plant Sci*., **5**, 390 (2011)
[204] M. Mitoshi, I. Kuriyama, H. Nakayama, H. Miyazato, K. Sugimoto *et al*., *J. Agric. Food Chem*., **60**, 11343 (2012), https://doi.org/10.1021/jf303377f
[205] M. Akhlaghi, G. Shabanian, M. Rafieian-Kopaei, N. Parvin, M. Saadat *et al*., *Brazilian J. Anesthesiol*., **61**, 702 (2011), https://doi.org/10.1016/S0034-7094(11)70079-4
[206] N. Heydari, M. Abootalebi, N. Jamalimoghadam, M. Kasraeian, M. Emamghoreishi *et al*., *Complement. Ther. Clin. Pract*., **32**, 1 (2018), https://doi.org/10.1016/j.ctcp.2018.04.006
[207] A. De Moraes Pultrini, L. Almeida Galindo and M. Costa, *Life Sci*., **78**, 1720 (2006), https://doi.org/10.1016/j.lfs.2005.08.004
[208] G. A. Castillo-Herrera, L. J. Farías-Álvarez, J. A. García-Fajardo, J. I. Delgado-Saucedo, A. M. Puebla-Pérez *et al*., *J. Supercrit. Fluids*, **101**, 81 (2015), https://doi.org/10.1016/j.supflu.2015.02.026
[209] M. Russo, I. Bonaccorsi, V. Inferrera, P. Dugo and L. Mondello, *J. Funct. Foods*, **12**, 150 (2015), https://doi.org/10.1016/j.jff.2014.11.008
[210] A. G. Saeed Mollayi, R. Zadali and M. Farzaneh, *Phytochem. Lett*., **13**, 290 (2015), https://doi.org/10.1016/j.phytol.2015.07.010
[211] Y. Zhao, H. Sun, L. Ma and A. Liu, *Int. J. Biol. Macromol*., **101**, 680 (2017), https://doi.org/10.1016/j.ijbiomac.2017.03.149
[212] J. R. Patil, G. K. Jayaprakasha, K. N. C. Murthy, M. B. Chetti and B. S. Patil, *Microchem. J*., **94**, 108 (2010), https://doi.org/10.1016/j.microc.2009.09.008
[213] R. Fekrazad, A. Poorsattar Bejeh Mir, V. Ghasemi Barghi and M. Shams-Ghahfarokhi, *Photodiagn. Photodyn. Ther*., **12**, 289 (2015), https://doi.org/10.1016/j.pdpdt.2014.12.009
[214] F. Yang, G. P. Wang, B. Jiang, Y. H. Liu, Y. Liu *et al*., *Physiol. Mol. Plant Pathol*., **83**, 17 (2013), https://doi.org/10.1016/j.pmpp.2013.03.001
[215] M. Sayyah, H. Boostani, S. Pakseresht and A. Malaieri, *Prog. Neuro-Psychopharmacol. Biol. Psych*., **33**, 1513 (2009), https://doi.org/10.1016/j.pnpbp.2009.08.021
[216] M. R. Heidari, E. M. Azad and M. Mehrabani, *J.*

Ethnopharmacol., **103**, 345 (2006), https://doi.org/10.1016/j.jep.2005.08.027
[217] B. Asghari, S. Mafakheri, M. M. Zarrabi, S. A. Erdem, I. E. Orhan *et al*., *South African J. Bot*., **120**, 191 (2018), https://doi.org/10.1016/j.sajb.2018.05.017
[218] S. F. Zohra, B. Meriem and S. Samira, *APCBEE Proc*., **5**, 546 (2013), https://doi.org/10.1016/j.apcbee.2013.05.091
[219] S. Feizi, E. Taghipour, P. Ghadam and P. Mohammadi, *Microb. Pathog*., **125**, 33 (2018), https://doi.org/10.1016/j.micpath.2018.08.054
[220] C. Wang, A. Pei, J. Chen, H. Yu, M. L. Sun *et al*., *J. Neurochem*., **121**, 1007 (2012), https://doi.org/10.1111/j.1471-4159.2012.07744.x
[221] H. Zuo, Y. Li, Y. Cui and Y. An, *Biomed. Pharmacother*., **95**, 679 (2017), https://doi.org/10.1016/j.biopha.2017.08.111
[222] A. S. Prudente, G. Sponchiado, D. A. G. B. Mendes, B. S. Soley, D. A. Cabrini *et al*., *Biomed. Pharmacother*., **93**, 852 (2017), https://doi.org/10.1016/j.biopha.2017.06.083
[223] P. F. Esteves, A. Sato, M. A. Esquibel, F. de Campos-Buzzi, A. V. Meira *et al*., *Lat. Am. J. Pharm.* **28**, 454 (2009)
[224] A. S. Prudente, A. M. V. Loddi, M. R. Duarte, A. R. S. Santos, M. T. Pochapski *et al*., *Food Chem. Toxicol*., **58**, 324 (2013), https://doi.org/10.1016/j.fct.2013.04.042
[225] J. Q. Yu, Y. L. Geng, D. J. Wang, H. W. Zhao, L. Guo *et al*., *Phytochem. Lett*., **28**, 59 (2018), https://doi.org/10.1016/j.phytol.2018.09.010
[226] J. Yang, J. Ren and A. Wang, *Phytochem. Lett*., **23**, 73 (2018), https://doi.org/10.1016/j.phytol.2017.10.005
[227] R. R. Bannuru, M. C. Osani, F. Al-Eid and C. Wang, *Semin. Arthritis Rheum*., **48**, 416 (2018), https://doi.org/10.1016/j.semarthrit.2018.03.001
[228] M. Taghizadeh, F. Maghaminejad, A. Mohammad, M. Rahmani and M. Mahboubi, *Arch. Gerontol. Geriatr*., **75**, 146 (2018)
[229] I. Kostova and T. Iossifova, *Fitoterapia*, **78**, 85 (2007), https://doi.org/10.1016/j.fitote.2006.08.002
[230] M. Maghrani, N. A. Zeggwagh, A. Lemhadri, M. El Amraoui, J. B. Michel *et al*., *J. Ethnopharmacol*., **91**, 309 (2004), https://doi.org/10.1016/j.jep.2004.01.008
[231] R. K. Dhiman and Y. K. Chawla, *Dig. Dis. Sci*., **50**, 1807 (2005), https://doi.org/10.1007/s10620-005-2942-9
[232] M. Pautasso, G. Aas, V. Queloz and O. Holdenrieder, *Biol. Conserv*., **158**, 37 (2013), https://doi.org/10.1016/j.biocon.2012.08.026
[233] M. El-Hefny, A. A. Mohamed, M. Z. M. Salem, M. S. M. Abd El-Kareem and H. M. Ali, *Sci. Hortic. (Amsterdam)*, **233**, 225 (2018), https://doi.org/10.1016/j.scienta.2018.01.046
[234] O. Kadioglu, S. Jacob, S. Bohnert, J. Naß, M. E. M. Saeed *et al*., *Phytomedicine*, **23**, 293 (2016), https://doi.org/10.1016/j.phymed.2016.01.004
[235] A. Bozicevic, M. De Mieri, A. Di Benedetto, F. Gafner and M. Hamburger, *Phytochemistry*, **138**, 134 (2017), https://doi.org/10.1016/j.phytochem.2017.02.028
[236] A. M. Pawlowska, F. Camangi, A. Bader and A. Braca, *Food Chem*., **112**, 858 (2009), https://doi.org/10.1016/j.foodchem.2008.06.053
[237] N. Hayder, I. Skandrani, S. Kilani, I. Bouhlel, A. Abdelwahed *et al*., *South African J. Bot*., **74**, 121 (2008), https://doi.org/10.1016/j.sajb.2007.10.001
[238] A. Chidouh, S. Aouadi and A. Heyraud, *Food Hydrocoll*., **35**, 733 (2014), https://doi.org/10.1016/j.foodhyd.2013.08.001
[239] A. Bouzabata, O. Bazzali, C. Cabral, M. J. Gonçalves, M. T. Cruz *et al*., *J. Ethnopharmacol*., **149**, 613 (2013), https://doi.org/10.1016/j.jep.2013.06.054
[240] M. H. Akhter and M. T. Khan, *J. Ethnopharmacol*., **11**, 275 (1984), https://doi.org/10.1067/mge.2001.118256
[241] W. Aidi Wannes, B. Mhamdi and B. Marzouk, *Food Chem*., **112**, 621 (2009), https://doi.org/10.1016/j.foodchem.2008.06.018
[242] W. A. Wannes, B. Mhamdi, J. Sriti, M. B. Jemia, O. Ouchikh *et al*., *Food Chem. Toxicol*., **48**, 1362 (2010), https://doi.org/10.1016/j.fct.2010.03.002
[243] P. Montoro, C. I. G. Tuberoso, S. Piacente, A. Perrone, V. De Feo *et al*., *J. Pharm. Biomed. Anal*., **41**, 1614 (2006), https://doi.org/10.1016/j.jpba.2006.02.018
[244] D. Csupor, A. Csorba and J. Hohmann, *J. Pharm. Biomed. Anal*., **130**, 301 (2016), https://doi.org/10.1016/j.jpba.2016.05.034
[245] A. Borah, R. Paul, S. Choudhury, A. Choudhury, B. Bhuyan *et al*., *CNS Neurosci. Ther*. **19**, 847 (2013), https://doi.org/10.1111/cns.12175
[246] N. Škottová, V. Krečman, D. Walterová, J. Ulrichová and P. Kosina, *Fac. Medica*, **141**, 87 (1998)
[247] N. Ahmad, B. H. Abbasi and H. Fazal, *Ind. Crop. Prod*., **49**, 164 (2013), https://doi.org/10.1016/j.indcrop.2013.05.004
[248] N. Nazir, N. Karim, H. Abdel-Halim, I. Khan, S. F. Wadood *et al*., *J. Ethnopharmacol*., **210**, 198 (2018), https://doi.org/10.1016/j.jep.2017.08.026
[249] N. B. Qin, C. C. Jia, J. Xu, D. H. Li, F. X. Xu *et al*., *Fitoterapia*, **119**, 83 (2017), https://doi.org/10.1016/j.fitote.2017.04.008
[250] S. Y. Zhu, N. Jiang, J. Tu, J. Yang and Y. Zhou, *Biomed. Environ. Sci*., **30**, 623 (2017), https://doi.org/10.3967/bes2017.083
[251] M. R.-K. Asadi-Samani, M. N. Kafash-Farkhad, N. Azimi, A. Fasihi and E. Alinia-Ahandani, *Asian Pac. J. Trop. Biomed*., **5**, 87 (2015), https://doi.org/10.1016/S2221-1691(15)30170-2
[252] A. Fondell, K. Edwards, L. M. Ickenstein, S. Sjöberg, J. Carlsson *et al*., *Eur. J. Nucl. Med. Mol. Imaging*, **37**, 114 (2010), https://doi.org/10.1007/s00259-009-1225-7
[253] S. S. Santos, A. Lorenzoni, N. S. Pegoraro, L. B. Denardi, S. H. Alves *et al*., *Colloid. Surfaces B Biointerf*., **116**, 270 (2014),

https://doi.org/10.1016/j.colsurfb.2014.01.011
[254] K. Li, E. Imre, A. S. His and B. Liu, *Chem. Soc. Rev*., **43**, 6570 (2014), https://doi.org/10.1039/C4CS00014E
[255] M. A. Augustin and Y. Hemar, *Chem. Soc. Rev*., **38**, 902 (2009), https://doi.org/10.1039/b801739p
[256] B. N. Estevinho, F. Rocha, L. Santos and A. Alves, *Trends Food Sci. Technol*., **31**, 138 (2013), https://doi.org/10.1016/j.tifs.2013.04.001
[257] A. Gonçalves, B. N. Estevinho and F. Rocha, *Trends Food Sci. Technol*., **51**, 76 (2016), https://doi.org/10.1016/j.tifs.2016.03.001
[258] I. T. Carvalho, B. N. Estevinho and L. Santos, *Int. J. Cosmet. Ind*., **38**, 109 (2016)
[259] B. N. Estevinho and F. Rocha, in "Biopolymers for Food Design", edited by M. Grumezescu and A. M. Holban, Elsevier Inc., 2018, pp. 191-222
[260] J. Aguiar, B. N. Estevinho and L. Santos, *Trends Food Sci. Technol*., **58**, 21 (2016), https://doi.org/10.1016/j.tifs.2016.10.012
[261] B. N. Estevinho and F. Rocha, in "Advances in Food Biotechnology", edited by R. V. Ravishankar, John Wiley & Sons, Ltd., 2016, pp. 593-606, https://doi.org/10.1002/9781118864463.ch36
[262] B. N. Estevinho and F. Rocha, in "Nanotechnology Applications in Food: Flavor, Stability, Nutrition and Safety", edited by A. E. Oprea and A. M. Grumezescu, Elsevier Inc., Oxford, United Kingdom, 2017, pp. 1-16, https://doi.org/10.1016/B978-0-12-811942-6.00001-7
[263] M. Cano-Sarabia and D. Maspoch, in "Encyclopedia of Nanotechnology", edited by B. Bhushan, Springer, 2015, https://doi.org/10.1007/978-94-007-6178-0
[264] K. G. H. Desai and H. J. Park, *Drying Technol*., **23**, 1361 (2005), https://doi.org/10.1081/DRT-200063478
[265] A. Jaworek, *J. Microencapsul*., **25**, 443 (2008), https://doi.org/10.1080/02652040802049109
[266] P. Chivero, S. Gohtani, H. Yoshii and A. Nakamura, *LWT - Food Sci. Technol*., **69**, 59 (2016), https://doi.org/10.1016/j.lwt.2015.12.064
[267] A. Kyriakoudi and M. Z. Tsimidou, *Food Chem*., **266**, 458 (2018), https://doi.org/10.1016/j.foodchem.2018.06.038
[268] H. Rajabi, M. Ghorbani, S. Mahdi, A. Sadeghi and G. Rajabzadeh, *Food Hydrocoll*., **51**, 327 (2015), https://doi.org/10.1016/j.foodhyd.2015.05.033
[269] S. A. Khatibi, A. Misaghi, M. H. Moosavy, A. A. Basti, M. K. Koohi *et al*., *J. Food Process. Preserv*., **41**, 1 (2017), https://doi.org/10.1111/jfpp.12955
[270] P. D. F. dos Santos, C. R. L. Francisco, A. Coqueiro, F. V. Leimann, J. Pinela *et al*., *Food Funct*., (2019), https://doi.org/10.1039/C8FO02431F
[271] M. S. El-Samaligy, N. N. Afifi and E. A. Mahmoud, *Int. J. Pharm*., **308**, 140 (2006), https://doi.org/10.1016/j.ijpharm.2005.11.006
[272] A. Visentin, S. Rodríguez-Rojo, A. Navarrete, D. Maestri and M. J. Cocero, *J. Food Eng*., **109**, 9 (2012), https://doi.org/10.1016/j.jfoodeng.2011.10.015
[273] L. De Souza, D. A. Madalena, A. C. Pinheiro, J. A. Teixeira, A. A. Vicente *et al*., *Adv. Colloid Interface Sci*., **243**, 23 (2017), https://doi.org/10.1016/j.cis.2017.02.010
[274] M. Fathi, A. Martin and D. J. McClements, *Trends Food Sci. Technol*., **39**, 18 (2014), https://doi.org/10.1016/j.tifs.2014.06.007
[275] C. E. Gumus, E. A. Decker and D. J. Mcclements, *J. Food Eng*., **207**, 90 (2017), https://doi.org/10.1016/j.jfoodeng.2017.03.019
[276] S. M. Jafari, Y. He, B. Bhandari, S. M. Jafari, Y. He *et al*., *Dry. Technol*., **25**, 1069 (2010), https://doi.org/10.1080/07373930701396758
[277] I. J. Joye and D. J. McClements, *Curr. Opin. Colloid Interface Sci*., **19**, 417 (2014), https://doi.org/10.1016/j.cocis.2014.07.002
[278] A. M. Abdul-Fattah, D. S. Kalonia and M. J. Pikal, *J. Pharm. Sci*., **96**, 1886 (2007), https://doi.org/10.1002/jps.20842
[279] J. Zhang, Q. Tang, X. Xu and N. Li, *Int. J. Pharm*., **448**, 168 (2013), https://doi.org/10.1016/j.ijpharm.2013.03.021
[280] T. Vasconcelos, B. Sarmento and P. Costa, *Drug Discov. Today*, **12**, 1068 (2007), https://doi.org/10.1016/j.drudis.2007.09.005
[281] C. R. L. Francisco, S. A. Heleno, I. P. M. Fernandes, J. C. M. Barreira, R. C. Calhelha *et al*., *Food Chem*., **245**, 845 (2018), https://doi.org/10.1016/j.foodchem.2017.11.098
[282] R. Shishir, in *Procs. Int. Conf. Electromagn. Interf. Compat*., 2016, pp. 1-4, https://doi.org/10.1109/INCEMIC.2016.7921513
[283] S. Y. Hundre, P. Karthik and C. Anandharamakrishnan, *Food Chem*., **174**, 16 (2015), https://doi.org/10.1016/j.foodchem.2014.11.016
[284] J. Weiss, E. A. Decker, D. J. Mcclements, K. Kristbergsson, T. Helgason *et al*., *Food Biophys*., **3**, 146 (2008), https://doi.org/10.1007/s11483-008-9065-8
[285] F. Tamjidi, M. Shahedi, J. Varshosaz and A. Nasirpour, *Innov. Food Sci. Emerg. Technol*., **19**, 29 (2013), https://doi.org/10.1016/j.ifset.2013.03.002
[286] R. Singh, N. Bharti, J. Madan and S. N. Hiremath, *J. Pharm. Sci. Technol*. **2**, 171 (2010)
[287] A. I. Bourbon, M. A. Cerqueira and A. A. Vicente, *J. Food Eng*., **180**, 110 (2016), https://doi.org/10.1016/j.jfoodeng.2016.02.016
[288] K. Alvani, X. Qi and R. F. Tester, *Starch - Stärke*, **63**, 424 (2011), https://doi.org/10.1002/star.201000110
[289] E. Assadpour, S. Jafari and Y. Maghsoudlou, *Int. J. Biol. Macromol*., **95**, 238 (2017), https://doi.org/10.1016/j.ijbiomac.2016.11.023
[290] V. M. Busch, A. Pereyra-Gonzalez, N. Šegatin, P. R. Santagapita, N. P. Ulrih *et al*., *LWT - Food Sci. Technol*., **75**, 227 (2017), https://doi.org/10.1016/j.lwt.2016.08.055
[291] M. Rezaul, I. Shishir, L. Xie, C. Sun and X. Zheng, *Trends Food Sci. Technol*., **78**, 34 (2018), https://doi.org/10.1016/j.tifs.2018.05.018

[292] D. Duchêne and A. Bochot, *Int. J. Pharm.*, **514**, 58 (2016), https://doi.org/10.1016/j.ijpharm.2016.07.030
[293] P. Shao, J. Zhang, Z. Fang and P. Sun, *Food Hydrocoll.*, **41**, 132 (2014), https://doi.org/10.1016/j.foodhyd.2014.04.003
[294] A. P. Rokhade, S. A. Agnihotri, S. A. Patil, N. N. Mallikarjuna, P. V. Kulkarni *et al.*, *Carbohyd. Polym.*, **65**, 243 (2006), https://doi.org/10.1016/j.carbpol.2006.01.013
[295] K. Nienaltowska, G. Perfetti, G. M. H. Meesters, F. Ronsse, J. G. Pieters *et al.*, *Powder Technol.*, **198**, 298 (2010), https://doi.org/10.1016/j.powtec.2009.11.026
[296] V. R. Babu, K. S. V. K. Rao and Y. I. Lee, *Polym. Bull.*, **65**, 157 (2010), https://doi.org/10.1007/s00289-009-0238-5
[297] S. Prasertmanakit, N. Praphairaksit, W. Chiangthong and N. Muangsin, *AAPS PharmSciTech.*, **10**, 1104 (2009), https://doi.org/10.1208/s12249-009-9305-3
[298] F. Naqash, F. A. Masoodi, S. A. Rather, S. M. Wani and A. Gani, *Carbohyd. Polym.*, **168**, 227 (2017), https://doi.org/10.1016/j.carbpol.2017.03.058
[299] J. Chen, W. Liu, C. Liu, T. Li, R. Liang *et al.*, *Crit. Rev. Food Sci. Nutr.*, **55**, 1684 (2015), https://doi.org/10.1080/10408398.2012.718722
[300] H. Madziva, K. Ã. Kailasapathy and M. Phillips, *LWT - Food Sci. Technol.*, **39**, 146 (2006), https://doi.org/10.1016/j.lwt.2004.12.015
[301] C. Chang, T. Wang, Q. Hu, M. Zhou, J. Xue *et al.*, *Food Hydrocoll.*, **70**, 143 (2017), https://doi.org/10.1016/j.foodhyd.2017.03.033
[302] A. Bernkop-Schnürch and S. Dünnhaupt, *Eur. J. Pharm. Biopharm.*, **81**, 463 (2012), https://doi.org/10.1016/j.ejpb.2012.04.007
[303] J. Liang, H. Yan, P. Puligundla, X. Gao and Y. Zhou, *Food Hydrocoll.*, **69**, 286 (2017), https://doi.org/10.1016/j.foodhyd.2017.01.041
[304] M. Santa-Maria, H. Scher and T. Jeoh, *J. Microencapsul.*, **29**, 286 (2012), https://doi.org/10.3109/02652048.2011.651494
[305] S. Najafi-Soulari, H. Shekarchizadeh and M. Kadivar, *J. Biomater. Sci. Polym. Ed.*, **5063** (2016), https://doi.org/10.1080/09205063.2016.1226042
[306] D. Alvarenga, S. Vilela, R. Victória, D. B. Fernandes, R. Antoniassi *et al.*, *Food Chem.*, **221**, 1522 (2017), https://doi.org/10.1016/j.foodchem.2016.10.141
[307] V. D. Prajapati, G. K. Jani, N. G. Moradiya and N. P. Randeria, *Carbohyd. Polym.*, **92**, 1685 (2013), https://doi.org/10.1016/j.carbpol.2012.11.021
[308] D. Dag, M. Kilercioglu and M. H. Oztop, *LWT - Food Sci. Technol.*, **83**, 86 (2017), https://doi.org/10.1016/j.lwt.2017.05.007
[309] V. Kaushik and H. Ã. Roos, *LWT - Food Sci. Technol.*, **40**, 1381 (2007), https://doi.org/10.1016/j.lwt.2006.10.008
[310] N. Devi, M. Sarmah, B. Khatun and T. K. Maji, *Adv. Colloid Interface Sci.*, **239**, 136 (2017), https://doi.org/10.1016/j.cis.2016.05.009
[311] A. Oancea, I. Aprodu, I. O. Ghinea, V. Barbu, G. Bahrim *et al.*, *J. Food Eng.*, **210**, 83 (2017), https://doi.org/10.1016/j.jfoodeng.2017.04.033
[312] A. F. Esfanjani, S. M. Jafari and E. Assadpour, *Food Chem.*, **221**, 1962 (2017), https://doi.org/10.1016/j.foodchem.2016.11.149
[313] Y. Levinson, S. Ish-Shalom, E. Segal and Y. D. Livney, *Food Funct.*, **7**, 1477 (2016), https://doi.org/10.1039/c5fo01111f
[314] K. K. H. Y. Ho, K. Schroën, M. F. S. Martín-González and C. C. Berton-Carabin, *Food Struct.*, **12**, 34 (2017), https://doi.org/10.1016/j.foostr.2016.12.001
[315] L. Deng, X. Kang, Y. Liu, F. Feng and H. Zhang, *Food Chem.*, **231**, 70 (2017), https://doi.org/10.1016/j.foodchem.2017.03.027
[316] G. Ninan, J. Jose and Z. Abubacker, *J. Food Process. Preserv.*, **35**, 143 (2011), https://doi.org/10.1111/j.1745-4549.2009.00467.x
[317] N. M. Hani, A. E. Torkamani, M. H. Azarian, K. Wa and S. Hawa, *J. Sci. Food Agric.*, **97**, 3348 (2016), https://doi.org/10.1002/jsfa.8185
[318] M. P. Rascón, C. I. Beristain, H. S. García and M. A. Salgado, *LWT - Food Sci. Technol.*, **44**, 549 (2011)
[319] Z. Yao, M. Chang, Z. Ahmad and J. Li, *J. Food Eng.*, **191**, 115 (2016), https://doi.org/10.1016/j.jfoodeng.2016.07.012
[320] L. Dai, C. Sun, R. Li, L. Mao, F. Liu *et al.*, *Food Chem.*, **237**, 1163 (2017), https://doi.org/10.1016/j.foodchem.2017.05.134
[321] F. Donsì, P. Voudouris, S. J. Veen and K. P. Velikov, *Food Hydrocoll.*, **63**, 508 (2017), https://doi.org/10.1016/j.foodhyd.2016.09.039
[322] L. Liao, Y. Luo, M. Zhao and Q. Wang, *Colloid. Surfaces B Biointerfaces*, **92**, 305 (2012), https://doi.org/10.1016/j.colsurfb.2011.12.003
[323] S. Sun, Y. Song and Q. Zheng, *Food Hydrocoll.*, **23**, 1054 (2009), https://doi.org/10.1016/j.foodhyd.2008.04.002
[324] R. Wang, Z. Tian and L. Chen, *Int. J. Pharm.*, **406**, 153 (2011), https://doi.org/10.1016/j.ijpharm.2010.12.039
[325] C. Finnie and B. Svensson, *J. Proteomics.*, **72**, 315 (2008), https://doi.org/10.1016/j.jprot.2008.12.001
[326] S. David and Y. D. Livney, *Food Hydrocoll.*, **57**, 229 (2016), https://doi.org/10.1016/j.foodhyd.2016.01.027
[327] A. Blanco-Padilla, A. López-Rubio, G. Loarca-Piña, L. G.Gómez-Mascaraque and S. Mendoza, *LWT - Food Sci. Technol.*, **63**, 1137 (2015), https://doi.org/10.1016/j.lwt.2015.03.081
[328] M. Aceituno-Medina, A. Lopez-Rubio, S. Mendoza and J. María, *Food Hydrocoll.*, **31**, 289 (2013), https://doi.org/10.1016/j.foodhyd.2012.11.009
[329] A. Reinkensmeier, S. Bußler, O. Schlüter, S. Rohn and H. M. Rawel, *FRIN*, **76**, 160 (2015), https://doi.org/10.1016/j.foodres.2015.05.009
[330] D. F. Cortes-Rojas, C. R. F. Souza, M. Chen and W. P. Oliveira, *Pharm. Dev. Technol.*, **23**, 1047 (2018),

https://doi.org/10.1080/10837450.2017.1314491
[331] M. Marsanasco, A. L. Márquez, J. R. Wagner, V. Alonso and N. S. Chiaramoni, *Food Res. Int.*, **44**, 3039 (2011), https://doi.org/10.1016/j.foodres.2011.07.025
[332] Y. Feng, C. Sun, Y. Yuan, Y. Zhu, J. Wan *et al.*, *Int. J. Pharm.*, **501**, 342 (2016), https://doi.org/10.1016/j.ijpharm.2016.01.081
[333] P. Robert, T. Gorena, N. Romero, E. Sepulveda, J. Chavez *et al.*, *Int. J. Food Sci. Technol.*, **45**, 1386 (2010), https://doi.org/10.1111/j.1365-2621.2010.02270.x
[334] R. Albrecht, G. Kresze and B. Mlakar, *Chem. Ber.*, **97**, 483 (1964), https://doi.org/10.1016/j.scienta.2006.01.030
[335] A. Amiri and N. Mobarakabati, *Int. J. Nutr. Food Eng.*, **11**, 331 (2017)
[336] F. Beyranvand, A. Gharzi, A. Abbaszadeh and R. M. Khorramabadi, *Inflam. Regen.*, **39**, 1 (2019), https://doi.org/10.1186/s41232-019-0090-4
[337] S. M. Jafari, K. Mahdavi-Khazaei and A. Hemmati-Kakhki, *Carbohyd. Polym.*, **140**, 20 (2016), https://doi.org/10.1016/j.carbpol.2015.11.079
[338] C. Dufresne, F. Cormier, S. Dorion, U. A. Niggli, S. Pfister *et al.*, *Enzyme Microb. Technol.*, **24**, 453 (1999), https://doi.org/10.1016/S0141-0229(98)00143-4
[339] F. Cormier, C. Dufresne and S. Dorion, *Biotechnol. Tech.*, **9**, 553 (1995), https://doi.org/10.1007%2FBF00152442
[340] H. S. Colas, W. Shi, V. S. N. Malleswara Rao, A. Omri and M. R. Mozafari, in *Procs. 2013 Int. Conf. Qual. Reliab. Risk, Maintenance, Saf. Eng., QR2MSE 2013*, **4**, 1997 (2013), https://doi.org/10.1109/QR2MSE.2013.6625972
[341] L. Keawchaoon and R. Yoksan, *Colloid. Surfaces B Biointerfaces*, **84**, 163 (2011), https://doi.org/10.1016/j.colsurfb.2010.12.031
[342] A. Mohammadi, M. Hashemi and S. M. Hosseini, *Innov. Food Sci. Emerg. Technol.*, **28**, 73 (2015), https://doi.org/10.1016/j.ifset.2014.12.011
[343] K. Khosravi-Darani, M. E. Khoosfi and H. Hosseini, *J. Food Saf.*, **36**, 515 (2016), https://doi.org/10.1111/jfs.12271
[344] C. M. Zamarioli, R. M. Martins, E. C. Carvalho and L. A. P. Freitas, *Brazilian J. Pharmacogn.*, **25**, 53 (2015), https://doi.org/10.1016/j.bjp.2014.11.010
[345] M. Gayatri, V. Roopadarshini, R. Kavyashree and C. S. Kumar, *Plant Cell Biotechnol. Mol. Biol.*, **6**, 89 (2005)
[346] Y.-D. Yan, J. A. Kim, M. K. Kwak, B. K. Yoo, C. S. Yong *et al.*, *Biol. Pharm. Bull.*, **34**, 1179 (2011), https://doi.org/10.1248/bpb.34.1179
[347] Y. Wang, Z. Lu, F. Lv and X. Bie, *Eur. Food Res. Technol.*, **229**, 391 (2009), https://doi.org/10.1007/s00217-009-1064-6
[348] A. Paradkar, A. A. Ambike, B. K. Jadhav and K. R. Mahadik, *Int. J. Pharm.*, **271**, 281 (2004), https://doi.org/10.1016/j.ijpharm.2003.11.014
[349] S. Saeidy, A. Nasirpour, G. Djelveh, A. Ursu, C. Delattre *et al.*, *Colloid. Surfaces A*, **560**, 114 (2019), https://doi.org/10.1016/j.colsurfa.2018.10.018
[350] J. Casadebaig, M. Jacob, G. Cassanas, D. Gaudy, G. Batlac *et al.*, *J. Ethnobiol. Ethnomed.*, **26**, 211 (1989), https://doi.org/10.1016/0378-8741(89)90069-x
[351] G. Tonon, M. Capuana and C. Rossi, *J. Hortic. Sci. Biotechnol.*, **76**, 753 (2001), https://doi.org/10.1080/14620316.2001.11511441
[352] S. Sharma, A. Shahzad, S. Mahmood and T. Saeed, *Trees*, **29**, 345 (2015), https://doi.org/10.1007/s00468-014-1114-y
[353] E. Yahyaoui, D. Casamento, D. Frasheri, A. M. D. Onghia and M. A. Germana, *Acta Hortic.*, **1187**, 93 (2017), https://doi.org/10.17660/ActaHortic.2017.1187.11
[354] B. Tamargo, L. Monzote, A. Pinon, L. Machin, M. Garcia *et al.*, *Medicines*, **4**, 38 (2017), https://doi.org/10.3390/medicines4020038
[355] N. K. Mohammed, C. P. Tan, Y. A. Manap, A. M. Alhelli, A. Shobirin *et al.*, *Powder Technol.*, **317**, 1 (2017), https://doi.org/10.1016/j.powtec.2017.03.045
[356] A. E. Edris, D. Kalemba, J. Adamiec and M. Pi, *Food Chem.*, **204**, 326 (2016), https://doi.org/10.1016/j.foodchem.2016.02.143
[357] H. M. Fahmy, E. E. S. Saad, N. M. Sabra, A. A. El-Gohary, F. F. Mohamed *et al.*, *Int. J. Pharm.*, **548**, 597 (2018), https://doi.org/10.1016/j.ijpharm.2018.07.012
[358] D. Kanakdande, R. Bhosale and R. S. Singhal, *Carbohyd. Polym.*, **67**, 536 (2007), https://doi.org/10.1016/j.carbpol.2006.06.023
[359] M. Ziaee and S. Moharramipour, *J. Pest. Sci.*, **87**, 691 (2014), https://doi.org/10.1007/s10340-014-0590-6
[360] R. Akhtar and A. Shahzad, *Asian Pac. J. Trop. Biomed.*, **7**, 855 (2017), https://doi.org/10.1016/j.apjtb.2017.09.010
[361] Y. Wu, L. Yi, E. Li, Y. Li, Y. Lu *et al.*, *Int. J. Biol. Macromol.*, **102**, 68 (2017), https://doi.org/10.1016/j.ijbiomac.2017.04.006
[362] M. Bernela, M. Ahuja and R. Thakur, *Eur. J. Pharm. Biopharm.*, **105**, 141 (2016), https://doi.org/10.1016/j.ejpb.2016.06.003
[363] C. Zeng, W. Jiang, X. Wang, M. Tan and J. Xing, *J. Pharmacogn. Phytochem.*, **5**, 30 (2016)
[364] C. Zeng, W. Jiang, M. Tan, X. Yang, C. He *et al.*, *Eur. J. Pharm. Sci.*, **85**, 123 (2016), https://doi.org/10.1016/j.ejps.2016.02.007
[365] A. Kardošová and E. Machová, *Fitoterapia*, **77**, 367 (2006), https://doi.org/10.1016/j.fitote.2006.05.001
[366] B. Wang, G. Yen, L. Chang, W. Yen and P. Duh, *Food Chem.*, **101**, 729 (2006), https://doi.org/10.1016/j.foodchem.2006.01.051
[367] P. N. Karaputugala, E. S. C. Edirisinghe, D. L. C. Fonseka and W. L. G. Samarasinghe, *Int. J. Sci. Technol. Res.*, **7**, 131 (2018)
[368] M. Rosaria, L. Crasci, C. Carbone, R. Patrizia, A. Maria *et al.*, *LWT - Food Sci. Technol.*, **62**, 169 (2015), https://doi.org/10.1016/j.lwt.2015.01.017

[369] R. Nazari-Vanani, N. Azarpira and H. Heli, *J. Drug Deliv. Sci. Technol.*, **47**, 330 (2018), https://doi.org/10.1016/j.jddst.2018.08.003
[370] M. Manconi, M. L. Manca, C. Caddeo, G. Sarais, A. Palmieri *et al.*, *Medicines*, **5**, 108 (2018), https://doi.org/10.3390/medicines5040108
[371] O. Gortzi, S. Lalas, I. Chinou and J. Tsaknis, *Eur. Food Res. Technol.*, **226**, 583 (2008), https://doi.org/10.1007/s00217-007-0592-1
[372] A. E. Musa and G. A. Gasmelseed, *Chemistry (Easton)*, **1**, 35 (2012)
[373] M. Barani, M. Mirzaei, M. Torkzadeh-Mahani and M. H. Nematollahi, *DARU J. Pharm. Sci.*, **26**, 11 (2018), https://doi.org/10.1007/s40199-018-0207-3
[374] K. D. Kanbargi, S. K. Sonawane and S. S. Arya, *Int. J. Food Prop.*, **20**, 3215 (2017), https://doi.org/10.1080/10942912.2017.1282516
[375] E. Halevas, C. M. Nday, E. Chatzigeorgiou, V. Varsamis, D. Eleftheriadou *et al.*, *J. Inorg. Biochem.*, **176**, 24 (2017), https://doi.org/10.1016/j.jinorgbio.2017.07.018
[376] A. Shojaii and M. A. Fard, *ISRN Pharm.*, **2012**, 510795 (2012), https://doi.org/10.5402/2012/510795
[377] M. Osanloo, A. Amani, H. Sereshti, M. Reza and F. Esmaeili, *Ind. Crop. Prod.*, **109**, 214 (2017), https://doi.org/10.1016/j.indcrop.2017.08.037
[378] M. S. El-Samaligy, N. N. Afifi and E. A. Mahmoud, *Int. J. Pharm.*, **319**, 121 (2006), https://doi.org/10.1016/j.ijpharm.2006.04.023
[379] G. D. Noudeh, F. Sharififar, E. Behravan and E. Mohajeri, *J. Med. Plant Res.* **5**, 5378 (2011)
[380] S. Fahimi, S. Momen, H. Kojoori, N. Dorri, L. Ara *et al.*, *Int. J. Pharm. Sci. Res.*, **9**, 1263 (2018), https://doi.org/10.13040/ijpsr.0975-8232.9(3).1263-67
[381] A. R. Sahu and S. B. Bothara, *Int. J. Res. Med.*, **4**, 94 (2015)