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Investigating a Number of Iranian Herbal Medicine, In the form of Capsule Regarding the Product Components, Active Ingredients, Pharmacological Effects and Antimicrobial Properties

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Research in the areas of processing and production of plants applied in pharmacology and pharmacy is one of the oldest cultural and scientific characteristics of Iranians. A look at the mythology of Shahnameh and history of Iran shows that the scientific infrastructure of ancient pharmacology began in ancient Iran. After the introduction of Islam to Iran, it gradually developed among Iranian scientists, and using plant treatments became institutionalized in popular culture. The prophetic hadith about the characteristics of Iranian scholarship is a decisive evidence of this fact. The recently published papers about Iranian herbal medicines effective in the treatment and prevention of diseases were searched. The extended use of herbal products and the widespread and unsparing nature of Iran with all its varieties of climate, especially the use of medicinal plants and modern herbal medicines, and the brilliant achievements of scientists from the distant past until now has motivated the Minister of Health and Medical Education in this respect. Thus, the processing and utilization of herbal medicines and efforts in innovation and offering useful drugs is increasing every day. It is clear that any development of quantity in this regard should necessarily be in pace with quality improvement, consider the new horizons of knowledge and research, and obey the highest international scientific standards and recognized values confirmed by the international scientific society. It is hoped that this pharmacopeia, which is based on the international guidelines and standards and represents the high level of quality of herbal medicines produced in the country, be considered by the medical community and have a beneficial and crucial role in the promotion of public health.

Keywords: Herbal, Medicine, Pharmacology, Antimicrobial properties.

Medicinal plants have particular importance in ensuring the health of communities, both in the treatment and prevention of diseases. Historically, plants have played an important role in community development and extensive research to find natural materials and herbal preparations have been done throughout history. The medicinal plants are component stocks of natural resources and much of countries have source of plants that number and diversity of plant species based on the geographical location of each region is different. In below, list of Iranian herbal medicines that are used in the form of capsules, are introduced) 49).

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Pygium affricanum

Product components

Pygium affricanum capsules have been prepared from the leaves and fruit extract of an

herb with the same name which is local in Africa. It contains amygdalin, hydrocyanic acid, and considerable amounts of phytosterol, which is composed of beta sitosterol and campesterol[1]

Pharmacological effects and mechanism of action

Phytosterol found in the skin of the plant are the main cause of its therapeutic properties. In addition, by inhibiting the enzyme 5-alpha reductase, it prevents the conversion of testosterone into dihydrotestosterone which causes enlargement of the prostate gland. The recommended dose of the extract in pharmacological studies was reported 100 to 200 mg per day.

Antimicrobial properties

Several clinical studies have shown this drug's anti-inflammatory effects[2] and this herbal medicine is effective on a few fungi for example *Candida spp* and *Malassezia* species with form Soft Gel[3] .

Tanamigrain

Active ingredients

Tanamigrain capsules contain 125 mg of powdered Chrysanthemum parthenium (equivalent to at least 0.2% parthenolide).

Possible mechanism of action

Chrysanthemum parthenium probably acts through inhibition of granule secretion in blood platelets and neutrophils and thereby prevents migraine. It may also inhibit the release of prostaglandins (with a different mechanism from the mechanism of Cyclooxygenase inhibition)[4].

Antimicrobial properties

Antibacterial properties of the essential oil on fourteen pathogenic bacteria were determined by using broth dilution and well diffusion agar methods.

According to results of the studies, the chloroformic extract of *C. parthenium* at a concentration of 100 mg/ml after seven days has the highest effect in the treatment of *G. lamblia* infection in mice Balb/c[5]. This herbal medicine has antiprotozoal activity on *Trypanosoma cruzi* and *Leishmania sp*[6,7]

Gingiton

Product components

Each capsule contains 365 mg of dried ginger powder which is equivalent to 1.5% volatile oil.

Active ingredients

Includes gingerol, zingerone, shagaol, cineole geraniol, linalool, and oleoresins.

Pharmacological effects and mechanism of action

This drug has a systemic mechanism. The anti-nausea effects of ginger impact the gastrointestinal tract through the topical effects of the drug. Thus, it decreases severe gastrointestinal contractions which are effective factors in motion sickness, and nausea and vertigo. In addition, it also acts by preventing auditory impulses from reaching the automatic centers of the brain.(8)

Ginsin

Product components

Each capsule contains 250 mg of granular powdered rhizome ginseng.

Active ingredients

Ginseng active ingredients, which are biologically active and complex, are triterpenoid saponins called ginsenosides. Other constituent materials are: Panasen, beta sitosterol, low-molecular-weight polysaccharides, B vitamins, and different flavonoids.

Pharmacological effects and mechanism of action

Documentary evidence showed that ginseng has multiple pharmacological effects including anti-fatigue effects (physical and mental booster).[1] Experimental studies have shown that many anti-fatigue effects of ginsin are related to the stimulant effect of ginseng on the central nervous system. The effects are not related to ginsenosides, but depend on other compounds such as Panasen (peptidoglycan) vanillic acid, and salicylates, which have antioxidant properties and anti-fatigue effects in animals. It had been reported that ginseng has hormone-like effects, reduces cholesterol, intensifies vasodilatation, and anti-anxiety and anti-depression effects. Many clinical experiences demonstrate the power of ginseng extract and ginsenosides on enhancing learning and memory and physical activity[9].

Antimicrobial properties

The active ingredients of this drug increase resistance to infection.[9]According to results of the studies, this herbal medicine has antibacterial, antifungal and antiviral activity on bacteria , fungus and virals[10].

Zintoma

Product components

Each capsule contains 250 mg of ginger rhizome granular powder.

Pharmacological effects and mechanism of action

Preliminary studies on laboratory animals have approved the antiemetic effect of ginger. The antiemetic effect of 1.88 g ginger powder and the effect of 100 mg dimenhydrinate and placebo were studied on the symptoms of motion sickness of 36 people. It showed that the effect of ginger is superior to dimenhydrinate. Another study conducted on 1,489 tourist volunteers showed that ginger prevents nausea and vomiting during sea trips. Almost 80% of the subjects who took 250 mg of ginger 2 hours before departure showed no complication[11] The effect of ginger had been studied on the most severe nausea and vomiting of pregnancy. Another study shows that ginger reduces the pain of rheumatoid arthritis, osteoarthritis, and muscular discomfort[12]

Antimicrobial properties

It was proven that the anti-inflammatory effect of ginger occurs through inhibition of the production of prostaglandins and leukotrienes[13]. The results showed that ethanolic extract of ginger gave the widest zone of inhibition against the tested organisms. *Pseudomonas aeruginosa* was more sensitive to the extracts of ginger compared to other organisms. This plant had antibacterial activities on the gram negative test organisms but not effective on the gram positive test organism. Ginger extracts produced marked inhibitory effect on the test organisms. Thus it can be used widely in folk medicine in this regard[14].

Sedamin

Product components

Each capsule contains 530 mg of granules of processed *Valeriana officinalis* root powder.

Pharmacological effects and mechanism of action

Sedative effects of valerian have been clearly approved in animal experiments. These effects are related to volatile oils including valerenal, valerenic acid, and valepotriate compounds. Other studies have shown that valerenic acid causes a general weakening of the nervous system and has a phenobarbital-like effect on the brain. Biochemical studies also indicate that valerenic acid inhibits the enzymatic system, is responsible for the catabolism and degradation of gamma-aminobutyric acid (GABA), and increases GABA concentrations in brain tissue. GABA concentration in the brain causes a reduction in the activity of different brain nuclei, and thus, causes sedation. Valerenal and valerenic acid are the most potent sedative compounds of valerian. The sedative effects of valerian in humans have been demonstrated by numerous studies. This medication is effective for all disorders associated with insomnia. In a randomized clinical study on 100 patients for 2 weeks, it was shown that valerian is more effective than diazepam. (15) In addition, recent studies have related the sedative properties of valerian to its high concentration of glutamine. Glutamine is able to cross the blood-brain barrier; thus, it is absorbed by nerve endings and is then can be metabolized to GABA[16]

Garlicap

Product components

Each capsule contains 330 mg of dried garlic powder, equivalent to 0.3% to 0.2% allicin.

Pharmacological effects and mechanism of action

Lowering blood pressure and blood lipid and sugar, anti-atherosclerotic (anti-atherosclerosis), fibrinolytic, anticoagulant, antiseptic

Antimicrobial properties

Ethanol extracts obtained from *Valeriana officinalis* exerted significant antifungal activities against ten fungal strain *(Rhizopus, , Alternaria, Fusarium , Aspergillus*, *Penicillium , Cladosporium, Trichothecium, Trichoderma, Bisoclamis, Geotichum*). The finding demonstrated that the ethanol extract of *Valeriana officinalis* possess antioxidant and antifungal activities that might be a natural potential source of preservative used in food and allied industries[17].

Antimicrobial properties

Allicin, by blocking cysteine proteinase and alcohol dehydrogenase enzymes, reveals its antibiotic and anti-infective nature, because microorganism petrogen, through cysteine proteinase enzyme activity, attack tissues. In addition, alcohol dehydrogenase enzyme, by affecting the metabolism of microorganisms, increases the microbiological activity, and does not establish microbial resistance, due to the irreversible nature of enzymes blockage in comparison to allicin[18.] Very studies suggests that aqueous and alcholic garlic extracts have

significant antibactrrial (*Helicobacter pylori*[19], *Acinetobacter sp*[20], vancomycin- resistant *Enterococci*[21], Oral bacteria30 , *Enterococcus faecalis*[22], human enteric bacteria[23], *Salmonella typhimurium and Shigella dysenteric*[24], *Pseudomonas aeruginosa*[25], multidrug-resistant *Streptococcus mutans*[26], *Mycobacterium avium* and *Mycobacterium tuberculosis*[27]. Garlic extract in invitro studies is more than Nystatin, Amphoteracin and Clotrimazol, on Pathogenic Yeasts and Dermatophytes[28-30] . Results of many studies have shown that garlic extract have significant antiparasite *Toxoplasma gondii*[31], Leishmania *major*[32], *Trypanosoma cruzi*[33].

Traditional applications of garlic extracts in treatment of many viral diseases (HSV I, CMV) and its valuable medicinal and herbal components could provide a context for scientists to develop plant-derived medications such as antibiotics, sedatives and diabetes treating drugs, and key to conducting clinical trials[34-36].

Livomarin

Product components

Livomarin capsules contain granules of dried fruit extract of milk thistle (Silybum marianum).

Active ingredients

Thistle fruits contain flavonolignans such as silibin, silychristin, silydianin, and their 2 and 3 dihydro derivatives. The total of these flavonolignans are called silymarin.

Pharmacological effects and mechanism of action

The human liver has several vital functions including metabolism, digestion, and detoxification of the body's waste. Any type of liver damage may cause changes in liver cells, and affect the functioning power of the liver. Since the release of toxins in lipid peroxidation are involved in different types of liver toxicity, the strong anti-oxidation effect of silymarin and silibin may justify their protective effects against various toxic agents on the liver. These two combinations destroy free radicals and prevent peroxidative processes involved in liver injury induced by tetrachlorocarbon, thallium, ethanol, paracetamol, and other toxins of the liver. Silymarin increases ribonucleic acid (RNA) polymerase enzyme activity in the nuclei of cells. It acts as a direct antioxidant and removes toxic free radicals[37]

Antimicrobial properties

Silymarin is effective in treating both acute and chronic hepatitis virus.In a study on 29 patients with viral hepatitis treated with silymarin, it has been shown that silymarin dramatically impacts increased parameters of these patients such as bilirubin and serum liver enzyme levels compared with the placebo group[38] Extracts obtained and essential oils from *Lavandulastoechas*[39]and *Salvia officinalis*[40] *and Salvia macrochlamysBoiss*[41] exerted significant antibacterial activities against 4 bacteria strain(*staphylococcus* aureus ,E. Coli PTCC1039, Sh.flexneri PTCC 1234, *K.pneumoniae PTCC 1053*) and anticandida (C.albicans PTCC 5027 , Candida sp.)[39-41].

Memoral

Product components

Each Memoral capsule contains 360 mg alguem resin Boswellia and 36 mg of granola of ginger root powder.

Pharmacological effects and mechanism of action

Essences available in Boswellia have a relaxant effect on vascular muscles, especially cerebral vessels, and thereby relieve spasms and coronary stenosis, thus, resulting in the better flow of blood to tissue cells[42]. On the other hand, Boswellic acid derivatives are very active in terms of pharmacology and specifically inhibit endogenous leukotrienes synthesis. Thus, the use of Boswellia has positive effects on memory and curing amnesia. It is also effective in treatment of a number of diseases, including rheumatoid arthritis, allergic reactions, chronic bronchial asthma, and psoriasis. In recent years, extensive studies have been done on Boswellia, and it has been suggested for curing gastric, liver, and spleen cancer, and abdomen and brain tumors[43,44] In addition, Boswellia resin has antispasmodic and sedative effects and is useful for external use in treating ulcers and skin rash[45].

Antimicrobial properties

Results of studies have shown that *Gum olibanum* extract have significant.

Antibacterial (*E.coli, S.aureous, P.mirabilis*) and antifungal (*C.albicans*)[46] The antimicrobial effect *in vitro* of aqueous and ethanolic extracts of ginger (*Zingiber officinale* Roscoe*)* was assayed against *Staphylococcus aureus; Bacillus spp., Escherichia coli* and *Salmonella spp.* The aqueous and ethanolic extracts of garlic and ginger singly did not inhibit any of the test organisms. The highest inhibition

zone of 19 mm was observed with a combination of extracts on *Staphylococcus aureus. Salmonella spp* were resistant to almost all the extracts except lime[47]**.** Seven components were identified from the separation of ginger extracts by HPLC. The two extracts had antimicrobial activity; methanol extract was superior than n-hexane extract against the same tested micro- organisms. The results of studies revealed that this plant possesses some antibacterial (*Staphylococcus epidermidis, Staphylococcus aureus,Klebsiella sp., Escherichia coli, Proteus sp. Enterococcus sp., Pseudomonas fluorescent and antifungal (Candida albicans*) properties as antibiotics and antifungal, therefore they can be used as a potential source of active ingredients for food, pharmaceutical industry or preservatives[48-51]

Menstrugol

Product components

Each capsule contains about 500 mg of dry extract of anise, celery, and saffron

Active ingredients

Anethole, estragole, methylchavicol, apiin, apigenin, myristin, limonene, cineole, safranal, crocin, and picrocrocin[52].

Pharmacological effects and mechanism of action

Anti-spasmodic and anti-spasmodic pain effects of volatile essential oil (some active ingredients of Menstrugol) have long been proven. Pharmacological and clinical studies have confirmed this effect. Numerous clinical studies have proven the synergistic effect of the blend of essential oils. Anethole present in anise fruit is the main cause of its anti-spasmodic effect. Its effect on the smooth muscle is due to the effect of calcium metabolism. It reduces tonicity and severity of gastrointestinal contractions. This substance, in terms of chemical structure, is very similar to catecholamines adrenaline, noradrenaline, and dopamine[52]. These effects have been frequently demonstrated in clinical trials[53].

Antimicrobial properties

Cytotoxicity, antibacterial and anticandidal activities of seven common essential oils including anise *Pimpinella anisium* L., black cumin *Nigella sativa* L., caraway *Carum carve* L., clove *Syzgium aromaticum* L., cumin *Cuminum cyminum* L., fennel *Foeniculum graveolens* Mill, and rosemary *Rosmarinus officinalis* L. were investigated against *Artemia salina* (Brine shrimp), two Gram-positive bacteria *Staphylococcus aureus* and *Bacillus subtilis,* four Gram-negative bacterial strains *Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris* and *Pseudomonas aeruginosa* and two yeasts, *Candida albicans* and *Candida tropicalis.* The oils of clove and rosemary showed strong cytotoxic activity against the nauplii of brine shrimps. The oils of black cumin, clove, fennel and rosemary exhibit antimicrobial activity. Clove oils gave broad spectrum antimicrobial activity. The sensitivity of minimal inhibitory concentration assay of clove oil against the tested yeast was comparable to that of the cytotoxicity assay. The biological activity of those steam- distilled oils were heat-resistant as they did not lose activity after autoclaving[54]. : Results of studies have shown that *Kelussia odoratissima* extract have significant antibacterial (*E.coli, Listeria innocua*, *Bacillus cereus*)[54-56].

Valerian

Product components

Each capsule contains 350 mg of valerian root powder containing 0.4% effective material (valepotriate).

Antimicrobial properties

The rhizome and root extracts of Valeriana wallichii DC in various solvents were investigated for its antimicrobial effect. The crude extracts were tested against gram positive Staypholococcus aureus, Staypholococcus epidermidis and gram negative Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis bacteria and fungi Aspergillus niger, Candida albicans, M. furfur to find out their antimicrobial activity using agar diffusion method. Ethanol and Methanol solvent extracts showed significant antimicrobial activity ranging from 13-18mm diameter of zone of inhibition especially against fungal pathogens as compared to bacterial pathogens[57,58].

Hypicum

Product components

Hypicum capsules are made from the dried extract of Hypericum.

Active ingredients

The most important active ingredients of hypericum are hypericin and pseudohypericin. Other substances found in this plant are flavonoids, phenolcarboxylic acid, caffeic acid, chlorogenic and gentisic acid[59].

Pharmacological effects and mechanism of action

Hypericum extract has numerous effects, which have been demonstrated through laboratory and clinical experiences. It produces antidepressant effects. Among the hypotheses about depression, the brain amines hypothesis has been accepted. According to this hypothesis, depression is due to lack of action of brain amines such as serotonin, catecholamines, and dopamine. These chemical mediators in the brain neurons are stored in granules. After stimulation of neurons, these chemical mediators are released into the neural nodes. Most antidepressant medication increase these nuclei of the brain amines, or inhibit neuronal return or metabolizing enzymes (MAO)[60]. Several studies have shown that extracts of Hypericum inhibit different types of A and B isoenzymes and monoamine oxidase (MAO) enzyme. As a result, the effect of the chemical mediators of serotonin, norepinephrine, and dopamine in the brain nuclei increases; thus, mood is improved and depression relieved (61) Later it was found that in addition of hypericin, flavonoids present in the plant also inhibit the mentioned enzymes[1].

Antimicrobial properties

Results of studies have shown that *Hypericum* extract have significant

Antibacterial *(E.coli, S.aureous, P.mirabilis, P.vulgaris , S.epidermidis, S.saprophyticus, Sarcina lutea*, *L.monocytogenes, B.subtilis, B. mycoides, M. phlei, C.michiganes, E. faecalis, E.faecium, E.durans, Ps.aeruginosa, Sal.choleraesuis, Sh.flexneri, K.pneumoniae, C. freundii, E.aerogenes and antifungal (C.albicans , P.crysogenum, F.avenaceum, Mucor.plumbeum)* antiviral (HSV I, HSV II, HIV and Orthomyxo viruses)[62].

Herbilax

Antimicrobial properties

Cassia senna leaves belonging to the family Fabaceae have been investigated for the presence of its secondary metabolites and evaluation of biological activities of the crude extracts with special emphasis to the antimicrobial activity, cytotoxic activity and thrombolytic activity. The antimicrobial activities of n-hexane, chloroform, ethyl acetate & methanolic extracts of *C. senna* leaves were screened against gram(+) bacteria (*Bacillus cereus*, *Bacillus megaterium, Bacillus subtilis* , *Staphylococcus aureus*) and gram(-) bacteria (*Escherichia coli* , *Vibrio mimicus* , *Pseudomonas aeruginosa , Shigella boydii, Salmonella paratyphi, Salmonella typhi)* and three fungi (*Sacharomyces cerevacae*, *C.albicans , Aspergillus niger*) by 'disc diffusion method'. The methanol extract possesses no antimicrobial activity but chloroform and n-hexane fractions exhibited moderate to less activity against some organisms tested compared with the standard antibiotic Kanamycin[63].

The disk diffusion assay and the minimum inhibitory concentration (MIC) assay using serial tube dilution technique were employed in the study by Sangetha *et al.* to investigate the antibacterial potency of *C. spectabilis*. The bacteria studied included *Proteus mirabilis*, *Staphylococcus aureus*, *Bacillus thuringiensis*, *Escherichia coli*, *Salmonella typhi*, *Micrococcus sp.*, *Enterobacter aerogenes*, *Bacillus subtilis*, *Azospirilium lipoferum*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa.* Overall, the leaf, flower, stem and pod extracts showed significant antibacterial activity against both Gram-positive and Gram-negative bacteria when compared to chloramphenicol which was used as a positive control. The *C. spectabilis* leaf extract was the most active one and it inhibited the growth of all the bacterial strains tested, specifically *Micrococcus sp.* (35 mm), *Staphylococcus aureus* (30 mm) and *Bacillus subtilis* (30 mm). As for the MIC assay, the MIC values against these Gram-positive and Gram-negative bacteria ranged from 0.195 to 50.000 mg/mL. The MIC results also indicated that the leaf extract is effective against Gram-positive bacteria at a lower concentration (0.195 mg/mL for *Bacillus subtilis*) compared to Gram-negative bacteria (50.000 mg/mL for *Pseudomonas aeruginosa*).

Furthermore, Subramanion *et al*[64] also reported the antimicrobial properties of various extracts namely acetone, *n*-hexane, dichloromethane, ethyl acetate and methanol leaf extract against Gram positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram negative bacteria (*Escherichia coli*, *Salmonella typhi* and *Pseudomonas aeroginosa*). They determined the MIC, and minimum bactericidal concentration (MBC) by using a microdilution assay. In their study the methanol extract showed the highest yield (14.12%) followed by

dichloromethane (8.37%), acetone (6.66%), ethyl acetate (4.76%) and n-hexane (1.80%). They also reported that the acetone and methanol extracts showed good antimicrobial activit, with MIC values ranging from 0.625 to .5 mg/mL and MBC values ranging from 1.25 to 5 mg/mL. The MIC and MBC values of these extracts were 10 to 80 times less potent than standard antimicrobial drugs, Amoxicillin and Miconazole nitrate they used in their study.

The methanolic extracts of the *C. spectabilis* leaves, flowers, stem and pods were evaluated for their antifungal activity against Saccharomyces *cerevisiae and Aspergillus* (64). The antifungal activity of the *C. spectabilis* leaf extract on *Candida albicans* was studied and the zone of inhibition obtained was 16 mm, compared to miconazole nitrate (30 µg/mL) which had a zone of 21 mm.

Table 1. List of Iranian herbal medicines that are used in the form of capsules

Row	Product name	Dosage form	Laboratory	Therapeutic effect
1	Pygium affricanum	Soft Capsule	Zahravi	Anti-prostate hyperplasia
2	Tanamigrain	Capsule	Zahravi	Anti-migraine
3	Gingiton	Capsule	Herbi Darou	Preventing motion sickness
4	Ginsin	Capsule	Gol Daru	Tonic
5	Zintoma	Capsule	Gol Daru	Preventing motion sickness
6	Sedamin	Capsule	Gol Daru	Sedative, hypnotic
7	Garlicap	Capsule	Herbi Darou	Lowering blood pressure, lowering blood fat
8	Livomarin	Capsule	Darou Pakhsh	Adjuvant treatment of liver toxicity
9	Memoral	Capsule	Gol Daru	Treatment of cerebral blood flow restriction
10	Menstrugol	Capsule	Gol Daru	Menstrual pain
11	valerian	Capsule	Herbi Darou	Sedative
12	Hypicum	Capsule	Darou Pakhsh	Antidepressants, sedatives, anti-migraine
13	Herbilax	Capsule	Herbi Darou	Laxative and stimulant laxative

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