IJBPAS, October, 2014, 3(10): 2461-2486

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

AN INVESTIGATION OF IRANIAN HERBAL MEDICINE, IN THE FORM OF TABLET, REGARDING THE PRODUCT COMPONENTS, ACTIVE INGREDIENTS, PHARMACOLOGICAL EFFECTS, AND MECHANISM OF ACTION

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ABSTRACT

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. 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 mentioned hadith which is well known among scholars and researchers states: "Even if knowledge is in the Pleiades, Iranians can gain it".

It should be noted that manufacturers of medicines and herbal products were able to form an association and by achieving unity and comprehensive scientific and research corporations increased their efforts in the area of improving the quality of herbal medicines. Thereby, it has benefited from the cooperation and diligent assistance of medical deputies, respected officials of plant department and control laboratory, and the ministry of Health, Treatment, and Medical Education. One of the significant and beneficial results which have been obtained from this cooperation include the editing of the pharmacopeia of herbal medicines of Iran under the supervision of Dr. Faribourz Moattar, with the cooperation of the board of drug and herbal product manufacturers. 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, Iranian, Laboratory

INTRODUCTION

List of herbal medicines in Iran that can be used in tablet form

1. (Aphrodite)

Product components: Each tablet or each 2 mm of drop contains the dry extract of the following herbs: 1. 40 mg Tribulus terrestris fruit; 2. Ginger 12.27 mg; 3. Saffron 3 mg; and 4. Cinnamon 11 mg.

Active ingredients: The most important ingredients in the order of their existence are: Tribulus Terrestris, saponin steroid, diosgenin, yamogenin, creston, kaempferia ginger, Zein J. Byrne, bisabolene, Flandren, aluzaine (shogaol), Saffron, crocin, crocetin and Esherishia Darpyn, Cinnamic aldehyde, and phenols (eugenol, Safrole, and PENn) **[1, 2]**.

Pharmacological effects and mechanism of action: The physiologic mechanism of penile erection involves release of nitric oxide (NO) in the corpus cavernosum during sexual stimulation. Nitric oxide activates guanylyl cyclase enzymes, resulting in increased levels of cGMP, leading to penile vasodilatation, and increases its blood circulation. This mechanism also increases women's sexual desire. Herbal active ingredients especially saponins, essential oils, and steroids used in Aphrodite products are effective in eliminating impotency, and with the mentioned mechanism, they cause vasodilatation and accumulation of blood in the penis, resulting in erection. It also increases sexual desire and prevents premature and incomplete ejaculation and leads to a satisfactory sexual experience **[1, 3]**. Several clinical studies have shown that saponins in Tribulus terrestris increased sperm count. Thus, it can be effective for patients who suffer from some degree of infertility due to low sperm count. In vitro studies have shown that the essence of this herb increases sperm motility and vitality; saponins increase the amount of LH hormone and thereby increase the amount of testosterone in the body. It is shown that Tribulus terrestris used in pharmaceutical formulations increases sexual desire in women and stimulates ovulation process **[4]**.

2. Agnugol

Product components: Each coated tablet contains extracts of dried fruits of Vitex (agnus castus) of 4.8-3.2 mg.

Active ingredients: Flavonoids (casticin, penduletin, chrysophanol d), alkaloids (vitisin, iridoid aucubin, agnozid), vitexin, and isovitexin are the most important flavonoids soluble in water **[5]**.

Pharmacological effects and mechanism of action: Vitex is a plant with phytoestrogen properties and is used during menopause. Today, it is evident that the active ingredients of this plant affect the pituitary gland and decrease prolactin secretion. This effect leads to stimulation of gonadotropin hormone LH and FSH, which is useful in the treatment of menstrual disorders. Investigations by several research groups have shown that the essence of this plant is linked to estrogen receptor and has estrogenic effect. This plant is capable of treating flushing fluid retention, depression, and other symptoms of menopause. High prolactin secretion may cause swelling and breast pain **[6]**. Modern studies have shown that the fruit of Vitex reduces the blood levels of prolactin by affecting dopamine receptors **[7]**. Extract of Vitex also removes lutein phase disturbance. This disorder causes shortening of the menstrual cycle which occurs due to inadequate secretion of progesterone, this is due to luteinizing hormone deficiency. Prolactin secretion from the anterior pituitary lobe is reduced by dopamine and thyroxine-releasing hormone (TRH) stimulates its secretion. Several clinical studies have shown that the extract of Vitex fruit treats perimenopausal syndrome (PMS), especially breast pain and inflammation **[8]**.

3. Althadin

Product components: Althadin tablets are prepared form Mentha Piperita and Althaea officinalis, which contains mucilage, oils, and substances such as sucrose, pectin, asparagine, betaine, lecithin, gum, and some fatty substances **[9]**.

Mechanism of action: Althadin tablets with mucilage and other effective ingredients have emollient properties, decreasing irritation and inflammation in the throat. It seems that it creates a membrane and a physical barrier to prevent the spread of stimulation.

Pharmacological effects: Althadin has emollient, anti-inflammatory, and antiseptic effects on irritation and inflammation of the lining of the throat and mouth, and induces sputum (expectorant effect) **[10]**.

4. Alicom

Formula: Alicom tablet is prepared from garlic powder Allium sativum.

Chemical composition: In addition to allicin which is the most noticeable compound of

garlic, other ingredients such as alien, ajoene, diallyl disulfide, diallyl disulfide, and other active ingredients have been recognized which cause the multiple properties of garlic **[11]**.

Mechanism of action: 1. Reduction of lipogenes endogenous or prevents their occurrence. 2. Increases fat breakdown and increases their excretion via the gastrointestinal tract. 3. Transfers lipids from tissue storage to the blood stream. 4. NADPH oxidation and thus inhibition of lipid synthesis is essential. 5. Garlic causes vasodilation of peripheral vessels, and with the increasing amount of peripheral arteries it lowers blood pressure. Moreover, due to its diuretic properties, it is effective in lowering blood pressure. 6. The antidiabetic effect of garlic is caused by increasing insulin, and this is applied by increased insulin secretion from pancreas, and also by the release of bonded insulin **[12, 13]**.

5. Allium-S

Active ingredients: Allium-S contains 400 mg garlic powder (Allium sativum), and is produced under the supervision of experts in Dineh Iran. In the chemical composition of garlic powder, in addition to allicin, which is the most noticeable compound, other ingredients such as alien, ajoene, diallyl disulfide, diallyl disulfide, and other active ingredients have been identified which are the cause of several garlic properties.

Pharmacological effects: An Allium-S tablet according to the active ingredients has numerous therapeutic properties that have been proved to lower cholesterol and triglycerides of the blood pressure and blood sugar. Furthermore, its fibrinolytic activity-enhancing effects and anticoagulant-induced inhibition of platelet aggregation have been confirmed.

Mechanism of action: 1. Reduction of lipogenes endogenous or prevents their occurrence. 2. Increases fat breakdown and increases their excretion via the gastrointestinal tract. 3. Transfers lipids from tissue storage to the blood stream, which is subsequently exerted. 4. NADPH oxidation and thus inhibition of lipid synthesis is essential. 5. Garlic causes vasodilation of peripheral vessels and with the increasing amount of peripheral arteries it lowers blood pressure and due to its diuretic properties, it is effective in lowering blood pressure. 6. The anti-diabetic effect of garlic is caused by increasing insulin, and this is applied by increased insulin secretion from pancreas, and also by the release of bonded insulin **[14, 15]**.

6. Echiherb

Product components: Each tablet contains latex of dried aerial parts of Echinacea Purpurea 114 mg.

Active ingredients: A significant number of ingredients in the Echinacea herb have been identified and isolated and the most important ones are: alkamides, polyalkamides caffeic acid derivatives (Echinacea cynarin, and chicoric acid), flavonoids (rutoside, quercetin, and camphrol), polysaccharide, and also other ingredients such as tussilagin and isotussilagin alkaloids **[16]**.

Pharmacological effects and mechanism of action: Numerous scientific studies and experiments show the effectiveness of Echinacea purpurea herb as an immune stimulant. Its immune-stimulating effect has three known mechanisms: 1. to activate the phagocytic function, and stimulate fibroblasts, and enhance respiratory function; 2. Increased activity and leukocyte interactions; and 3. Increased phagocytic activity **[1, 2]**. The leachate of Echinacea purpurea plant tissues dramatically increases the percentage of phagocytic function of human granulocytes and raises the phagocytosis of yeast particles in vitro conditions. Hyaluronidase activity interruption, cortical stimulation of the adrenal glands, and stimulation of properdin production (a serum protein that can act to neutralize bacteria and viruses) have been reported as results of the use of this plant. In addition, after treatment with this plant, an increase in interferon production has also been reported. Pharmacological activity of the plant Echinacea is related to its constituent materials and many essences **[17]**. The immune-stimulating effect of the plant is related to lipophilic alkamides and caffeic acid derivatives and is performed through phagocytosis of multi-core granulocytes **[18]**.

Contraindications and precautions: This drug should only be taken under a doctor's supervision for the following acute illnesses: Tuberculosis, calcinosis, lucosis, multiple sclerosis, AIDS, HIV infections, and autoimmune disorders **[19]**.

Precautions: Skin products of this herb can be used in the treatment of superficial wounds with small surface **[20]**.

7. Perforan

Product components: Each tablet contains about 160 mg of dry extract of goatweed or Hypericum perforatum.

Active ingredients: The main active ingredients of hypericum perforatum are hypericin and pseudohypericin. Other existing substances in the plant include: flavonoids, caffeic acid, chlorogenic acid, ferulic acid, and gentisic acid.

Pharmacological effects and mechanism of action: Hypericum extract has numerous

impacts, and their effectiveness has been demonstrated through laboratory and clinical experiences.

Anti-depressant effect: Among the underlying assumptions about depression, the intracerebral amine hypothesis has been best accepted. According to this hypothesis, depression is caused due to the lack of cerebral amines such as serotonin, catecholamines, and dopamine. These chemical mediators in the cerebral neurons are stored in granules. After neuronal stimulation these chemical mediators are freed into neural nodes. Most antidepressants increase these cerebral amines in brain cells, or by inhibition of neuronal return or by inhibition of metabolizing enzymes (MAO) **[21]**. Several studies have shown that extracts of Hypericum inhibit A and B isoenzymes of monoamine oxidase A (MAO). As a result of this effect, the chemical mediators of serotonin, norepinephrine, and dopamine increase in cerebral nuclei. This improves mood and relieves depression **[22]**. Later, it was found that in addition to hypericin, flavonoids existing in the plant also inhibit the mentioned enzymes **[23]**. At least two other mechanisms for the antidepressant effects of Hypericum have been proposed that include: modulation of interleukin-6 activity and interruption of serotonin return to the nerve **[24]**.

8. Prostatan

Product components: Each 1.5 ml drop and each coated tablet of Prostatan includes the following extracts: leaves and roots of nettle (28 mg), skinless pumpkin seeds (25 mg), chamomile (18 mg), tribulus terrestris fruit (22 mg), and anise fruit (17 mg).

Active ingredients: Nettle: flavonols, sterols, minerals (zinc); Anise: anatole; chamomile: quercetin, bisabolol; pumpkin seed: cucurbitin, phytosterols, minerals such as selenium and zinc; tribulus terrestris: steroidal saponins such as flavonoids; diocina and trrestris.

Pharmacological effects and mechanism of action: It seems that prostatic hyperplasia (BPH) is mainly related to changes due to aging in physiological sex hormones. Prostatic hyperplasia leads to the accumulation of dihydrotestosterone (DHT) in the prostate, which is more potent than testosterone. DHT has a higher tendency to androgen receptors than testosterone. In addition, through binding with androgen receptors of epithelial and prostate tissue, it causes enlargement and proliferation of its cells. This binding causes increased mRNA synthesis in the nucleus and ultimately cell growth **[25, 26]**. A Prostatan herbal product

with inhibitory effect on the 5-alpha reductase enzyme, which is the main factor for conversion of testosterone to dihydrotestosterone, decrease the concentration of this matter in serum, and thus stop the growth of prostate cancer, facilitates urine flow, and improve patient's condition. In addition to the above subjects, the ingredients in the root and leaf of nettle interfere in testosterone metabolism and reduce the binding power of globulin and testosterone. In addition, the sitosterol in nettle inhibits the synthesis of prostaglandins in the prostate tissue **[27]**. The most recent studies on the pharmacological properties of pumpkin seeds have shown that pumpkin seed extract is capable of inhibiting alpha-reductase enzyme. Active ingredients of the existing plants in Prostatan tablets and drops result in the relief of inflammation and prostate spasm. Thus, it eliminates the urinary symptoms caused by prostatic hyperplasia and improves urinating.

9. Tabokan

Product components: Each Tabokan tablet contains 40 mg of dried and purified extract of (50: 1) Ginkgo biloba leaves. The mentioned extract contains 22-27% flavonoid glycosides and is measured based on quercetin, and kaempferol. This extract also contains 5-7% terpene lactones, such as ginkgolic A, B, and C, and 2.6-3.2% bilobalide. Ginkgolic acid content in the extract was reduced to less than 5 ppm.

Pharmacology: According to the monograph published by the German Commission E, the following pharmacological effects have been demonstrated: 1. increased tolerance to hypoxia, particularly the cerebral tissue by inhibiting the development of cerebral edema and promoting its healing; 2. decreasing edema, cellular lesions in the retina, and neuroprotective properties (due to A and B ginkgolides and bilobalide); 3. Inhibiting muscarinic receptor and adrenergic receptor reduction related to age, and stimulation of choline uptake in the hippocampus; and 4. Improving blood flow, especially in the level of microcirculation, improving the rheological properties of blood, disabling toxic oxygen radicals (by the present isoflavones), and inhibiting platelet-activating factor (PAF) by ginkgolides **[28]**.

10. Ginkgo T.D.

Product component: Each tablet contains 40 mg of dried standardized extract of ginkgo biloba leaves.

Active ingredients: Ginkgo biloba leaves contain ginkgo flavone glycosides or ginkgo heterosides (flavonoid molecule binds to sugar), several terpene molecules (ginkgolides and bilobalide), and organic acids. The three

major flavonoids of this plant are quercetin, kaempferol, and Isorhamnetin. Other flavonoids consist of proanthocyanidins (hydro-catechin) biloptin, ginkgetin, isoginkgetin, catechin, B flavonoids, ginkgolic acid, and sterols.

Pharmacological effects and mechanism of action: Stimulation of the release of NO/EDRF and PGI_2, anti-oxidant activity of platelet-activating factor (PAF) antagonists, increase in releasing of chemical mediators, and interruption in the absorption of biogenic amines. It seems that flavonoids are responsible for anti-oxidant activity of the plant that forms one of the mechanisms of the pharmacological activities of extracts. Some effects of ginkgo biloba leaves are protection of the EDRF/NO system against superoxide anion, protection of endothelial cells against active oxygen species, macrophages against oxidative stress, and LDL against lipid peroxidation caused by superoxide radicals. In addition, the constituent materials of ginkgo biloba leaves have conflicting effects on PAF, and positive effect on metabolic lesions induced by cerebral ischemia, and noticeable antioxidant effects. The memory-enhancing effects of this plant have been approved in numerous clinical studies **[29]**.

11. Ginkogol

Product component: Each tablet of Ginkogol contains 40 mg dried standardized extract of ginkgo biloba leaf.

Active ingredients: Ginkgo biloba leaves contain ginkgo flavone glycosides or ginkgo heterosides (flavonoid molecule binds to sugar), several terpene molecules (ginkgolides and bilobalide), and organic acids. The three major flavonoids of this plant are quercetin, kaempferol, and isorhamnetin. The other flavonoids consist of proanthocyanidins (hydro-catechin) biloptin, ginkgetin, isoginkgetin, catechin, B flavonoids, ginkgolic acid, and sterols.

Pharmacological effects and mechanism of action: stimulation of the release of NO/EDRF and PGI_2 , anti-oxidant activity of PAF antagonists, increase in releasing of chemical mediators, and interruption in the absorption of biogenic amines. It seems that flavonoids are responsible for anti-oxidant activity of the plant that forms one of the mechanisms of the pharmacological activities of extracts. Some effects of ginkgo biloba leaves are protection of the EDRF/NO system against superoxide anion, protection of endothelial cells against active oxygen species, macrophages against oxidative stress, and LDL against lipid peroxidation caused by superoxide radicals. In addition, the constituent materials of ginkgo biloba leaves

have conflicting effects on platelet-activating factor PAF, a positive effect on metabolic lesions induced by cerebral ischemia, and noticeable antioxidant effects. The memory-enhancing effects of this plant have been approved in numerous clinical studies **[30]**.

12. Razin

Product component: Razin tablets contain 5% licorice extract (Glycyrrhiza glabra), and 0.5% fennel extract (Foeniculum vulgare).

Active ingredients: This tablet contains the active ingredients of glycerin, liquiritin, steroidal saponins, anethole, fenchone, and different flavonoids.

Pharmacological effects and mechanism of action: Flavonoids and Glycyrrhiza glabra saponin, by enhancing internal secretion, and resulting in increased secretion of prostaglandins, have an important role in protecting the gastric mucosa, inhibiting and improving of gastric ulcers and duodenum, and particularly preventing gastric acid secretion. The analgesic, antispasmodic, and carminative effects of Glycyrrhiza glabra have greatly increase due to the synergistic effect of volatile oil of fennel **[29]**.

13. Salvigol

Product component: Each coated tablet of Salvigol contains 100 mg of dried extract of aerial parts of Salvia officinalis.

Active ingredients: Young branches and leaves of Salvia contain 3%-8% tannins of the catechin group (Salvia tannin), phenolic acids, and 1%-3% flavonoids and volatile oils **[31, 32]**.

Pharmacological effects and mechanism of action: Salvia officinalis has long been used in the world of medicinal plants which is used. Laboratory and clinical studies have approved the anti-microbial, anti-fungal, and anti-viral effects of Salvia. This plant is able to powerfully inhibit the sweat secretion, and they attribute this impact to the tannins of the catechin group and phenolic acids such as Rosmarinic. Many clinical studies have been conducted in Germany that have proved that this species can inhibit the secretion of sweat.[33] In another study in an outpatient clinic, the impacts of dried extract of Salvia officinalis and its tea was studied on 80 patients with excessive sweat secretion for 4 weeks. 40 patients used 440 mg of dry extract (prepared by aqueous extraction method) equivalent to 2.6 g of dry leaves, and 40 other patients used plant infusion of 4.5 g of dry leaves daily. 50% reduction in sweat secretion was observed in both groups. However, the dried extract was more effective **[33]**.

In another study in the United Kingdom (1998) it was shown that Salvia inhibits sweat secretion in menopausal women **[34]**. Several

active terpene-like ingredients that have an antioxidant effect are the cause of its anti-microbial and other effects. It seems that the tannins with astringent effect and the anticholinergic effect of other compounds, including flavonoids and glycosides, reduce discharges.

14. Samilax

Product component: Each tablet contains about 154 mg (equivalent to 7.5 mg sennosides A and B).

Active ingredients: Its active ingredients include anthraquinones, such as glycosides dynatron, sennosides A and B (rhein dianthrones) which release sennidin, and sennosides C and D; free anthraquinones, including aloe emodin, chrysophanol, and rhein; and polysaccharides, including mucilage, galactose, mannose, and flavonoids. The main active ingredients of fennel are anethole and fenchone **[35]**.

Pharmacological effects and mechanism of action: Laxative effect of drugs containing anthraquinone has been well known for many years. It seems that anthraquinone glycosides are absorbed in the digestive tract, and the aglycones released during metabolism and excretion of large intestine lead to stimulation and increase in peristaltic movements of the intestine. However, it is also suggested that laxative effect of senna is related to enteric bacteria **[36, 37]**. Sennoside A with the help of enteric bacteria is converted into restored 8-glucosyltransferase rhein anthrone compound and then hydrolyzed and converted to rhein anthrone compound. Then, it is eventually oxidized producing sennosides A and B and especially affecting the large intestine and facilitating bowel evacuation. In addition, sennosides A and B stimulate the secretion of fluid into the large intestine **[38]**.

15. Senna-Lax

Product component: Senna-Lax is made up of dried extract of senna leaves (Cassia angustifolia) and coriander seeds (Coriandrum sativum). Each Senna-Lax tablet contains 9-11 mg active ingredient of Sennosides A and B.

Active ingredients: Senna therapeutic properties are due to anthraquinone glycosides (sennosides A and B). Sennosides A and B are metabolized by bacteria in the large intestine and are converted to active metabolites such as rhein. This material increases intestinal peristalsis and fluid secretion in the colon (by increasing the synthesis and secretion of prostaglandins, especially the colon), and facilitates defecation. In addition, histamine and 5-hydroxytryptamine (5-HT) present in senna have a laxative effect **[39]**.

16. C-Lax

Active ingredients: C-lax tablet contains 600 mg senna leaves (Cassia obovata) (equivalent to 15 mg sennoside B), and 3 mg Foeniculum vulgare extract.

In the chemical composition of senna leaves the most important active ingredients are crystalized anthraquinone glycosides called sennosides A and B. Their hydrolysis gives two molecules of glucose and aglycones named sennidin A and B which are produced from two units of rhein. Lower amounts of sennosides C and D exist, and their aglycones are comprised of one molecule of rhein and one molecule of aloe emodin. In addition, senna leaves contain minerals, mucilage, and flavone pigments such as kaempferol .

Mechanism of action: Free aglycones, which naturally exist in the composition of senna or are derived from the hydrolysis of glycosides after digestion by gastric juice, are absorbed in the small intestine. Beta-glucosidases are not hydrolyzed in the small intestine and are not absorbed, but after reaching the colon area they are hydrolyzed by beta-glucosidase and intestinal flora enzymes, and the obtained anthraquinones are restored. Therefore, the active form of compounds such as anthrone and anthranol are formed in the colon area. This reveals the cause of delay in the effect of the drug (6-12 hours) after administration. The active forms cause laxation in the colon area with increased mucus secretion and peristalsis. Absorbed free anthraquinone are excreted in the small intestine through the kidneys, causing the discoloration of urine. These compounds can also enter breast milk, saliva, and bile **[40]**.

17. Cynarchol

Active ingredients: Cynarchol tablets are prepared from the leaves of Cynara scolymus. This plant was exclusively and specifically developed in the fields of Dinah Industrial Complex, Iran, for the production of cynarchol tablets. Each tablet contains 250 mg dry extract of Cynara scolymus equivalent to 20 mg chlorogenic acid. Cynarchol extracts contain phenolic compounds such as cynarin, caffeic acid, chlorogenic acid, cynaropicrin, flavonoids (cynaroside and scolymoside), sterol, and minerals **[41]**.

Pharmacological effects and mechanism of action: This plant has been used since the old ages, and research has shown that Cynara scolymus increased bile secretion (Choleretic) and disposal (Cholagogue). It lowers cholesterol and blood lipids, enhances activity against liver toxicity, and resolves complications due to indigestion such as heaviness, flatulence, and nausea. This plant also has diuretic effects **[42]**. Previous research (1995) has shown that the extract of

Cynara scolymus has strong antioxidant effects.

18. Cynaroll

Product component: Cynaroll tablets contain 200 mg dried extract of artichoke leaves (Cynara scolymus) of the Compositae family. Artichoke extract contains 5% phenolic acids such as caffeic acid, chlorogenic acid, cynarin (dicaffeoylquinic acid) **[43]**.

Active ingredients: Artichoke contains the phenolic acids present in plants, particularly cynarin. Based on previous studies it was showed that after intraperitoneal injection of cynarin, bile secretion is increased (about 1.5 times), this activity was more lasting and more potent than sodium dehydrocholate and it is associated with increase in cholesterol secretion and solid matters in the bile. Moreover, unlike other chlorate compounds, after intravenous injection of cynarin no further impairment of liver excretory actions are observed **[44]**.

Pharmacological effects and mechanism of action: In a clinical study, it was found that daily doses of 900 mg of artichoke extract for 6 weeks reduced 12 to 15% of serum cholesterol. In another study on patients with hyperlipidemia after treatment with artichoke, 15% of their blood cholesterol decreased. In this study, it was also found that the HDL level increased. In another study 170 patients with symptoms such as nausea, dyspepsia, and biliary disorders were studied. After 6 weeks of treatment with artichoke (1.4 g artichoke extract daily) nausea and vomiting (95%), abdominal pain (75%), and cramp in the right area of the abdomen (25%) were improved. In addition, symptoms such as cramping and also fat intolerance significantly decreased. The total cholesterol decreased from 267 mg/dl to 228 mg/dl **[45]**.

19. Chicoridin

Active ingredients: Chicoridin is an herbal product which is produced from chicory root extract (Cichorium intybus), fenugreek seed (Trigonella foenum-graecum), and fennel extract (Foeniculum vulgare). Chicory root contains enough sugar, inulin, lactacin, lactucopicrin, and minerals (calcium, potassium, phosphorus, sodium, magnesium, and copper), vitamins B, vitamin C, vitamin K. Fenugreek seed contains sugars such as stachyose, galactomannan, lipids and sterols, proteins and nucleoproteins, phosphorus compounds such as lecithin, phitin, and nitrogen compounds such as choline and trigonelline, and the recent matter could be Vitamin PP (Nicotinamide). Fennel extract contains 50% to 60% anethole and also anisaldehyde, fenchone, and pinene **[46, 47]**.

20. Phytocold

Product component: Each tablet consists of the granular dry powder of the following material: Elderberry petals 50 mg, leachate of the aerial parts of Echinacea 75 mg, hollyhock root 80 mg.

Active ingredients: Active ingredients present in plants used in this product include: Echinacea: alkamides, polyalkenes, caffeic acid derivatives, polysaccharides, and glycosides. Elderberry: glycosides sambunigrin, Sambucine and flavonoids (quercetin). Hollyhock root: mucilage, flavonoids, coumarins, polyphenolic acids.

Pharmacological effects and mechanism of action: The Ekinase purpurea plant has several pharmacological properties that include: affecting enzymes which produce inflammation, proliferation and stimulation of the activity of multinucleate cells, protecting cells against damage caused by free radicals activating monocytes to produce cytokines. Laboratory experiments have shown that the active ingredient in alkamides in the extract of this plant interrupts cyclooxygenase enzymes and lipoxygenase enzymes. These two enzymes have a key role in the development of inflammation and thus contribute to the prevention and treatment of inflammation **[48]**. Moreover, it has been found that echinacea extract increases proliferation of multinucleated white blood cells, and thus it will increase the body's natural defenses. Other studies have shown that caffeic acid derivatives present in echinacea are able to prevent the damages caused by oxidized free radicals **[49]**. Preventive and treatment effects of echinacea plant along with two other plants in the formulation of fitocold tablets reduce the duration of cold treatment. Elderberry extract acts as an antiviral for cold and runny nose and is also effective in treating sinusitis. The hollyhock plant also has antibacterial effects against gram-positive and gram-negative bacteria. Mucilage compounds present in this plant act as emollient of the throat and respiratory tract and are effective in relieving dry coughs **[50]**.

21. Cratagol

Product component: Cratagol coated tablets contain 240 mg dry extract of flowers and leaves of Crataegus.

Active ingredients: Active flavonoids, especially anthocyanidin, and catechin flavonoids including quercetin glycosides.

Pharmacological effects and mechanism of action: The crataegus plant has a long history of use in the treatment of heart failure in particularly with digoxin. This drug may aggravate the effects of cardiac glycosides. This is done through inhibition of cAMP degrading enzymes (phosphodiesterase), and is linked to calcium channels **[51]**. In mild

forms of heart failure the efficacy of crataegus has been demonstrated through several double-blind clinical studies **[52]**. In one study, 30 patients with heart failure (stage 2 NYHA) were evaluated in a randomized manner. Treatment included standardized extract of crataegus containing 15 mg of oligomeric procyanidins. The treatment period was 8 weeks and 2 capsules a day were consumed. The group treated with crataegus extract, compared to the placebo group, showed significant cardiac changes that were measured with standard methods. Total flavonoids crataegus have inhibitory effect on positive enzymes and negative chronotropic **[53]**. The major flavonoids in crataegus increase coronary blood flow. Flavonoids crataegus was very efficient in maintaining collagen vascular and thus maintaing arteries against atherosclerotic plaques. This drug also has a mild diuretic effect **[54]**.

22. Garcin

Product component: Each tablet contains 300 mg of granules garlic powder.

Active ingredients: The active ingredients of garlic include: volatile oil; sulfide compounds (including alliin and allicin); and terpenes (including citral, geraniol, and linalool).

Pharmacological effects and mechanism of action: Garlic decreases blood cholesterol. This has been shown in animal studies and in patients with high blood pressure. This effect is related to diallyl disulfide which is the result of allicin breakdown **[55]**. Reduction of blood lipids and tissues in studies on animals treated with diets containing garlic powder or garlic oil, or allicin has been well approved. The beneficial effects of garlic are lowering of cholesterol, serum triglyceride, and low density lipoproteins (LDL), and increasing of HDL **[56]**. Its mechanism of action involves disruption of lipid synthesis and increased excretion of acidic and alkaline sterols **[57]**. The most important effect of garlic is its prevention and treatment of cardiovascular disease and atherosclerosis effect. Reduction of blood glucose and increase of insulin concentration in the blood is followed by the consumption of allyl propyl disulfide. In a clinical study with placebo group on patients with hypertension, 47 non-hospitalized patients with mild hypertension were treated with 600 mg of garlic powder for 12 weeks. After 8 weeks blood pressure had significantly decreased.

23. Gasterodin

Active ingredients: Gasterodin tablets are produced from 400 mg of licorice extract of Glycyrrhiza glabra, extracts of evergreen, Calendula off, hollyhock, and Althaea off. These tablets contain glycyrrhizin, liquiritin, saponin steroid, flavonoids, calendine,

mucilage, licorice extract which is due to the presence of glycyrrhizin. In preparing gasterodin tablets, an extract is used in which glycyrrhizin is reduced to the extent possible.

Pharmacological effects and mechanism of action: Acute and chronic gastritis are considered as the most common complications of gastric mucosal inflammation. Plants in gasterodin tablets have anti-inflammatory and anti-spasmodic effects. In addition, the flavonoids and saponins in these plants stimulate the production of and increase gastric protecting mucus secretion, and act as a protective barrier to prevent the effect of stomach acid on the gastric ulcer. Evergreens and hollyhock in these products, especially with their anti-inflammatory properties, are very effective in healing gastric and duodenal ulcers. Glycyrrhizin and its aglycon are two effective combination of licorice which increase the secretion of gastric mucosal and have an anti-heartburn effect. Antispasmodic effect of Gasterodin tablets are related to flavonoids. The essential oils in evergreens have strong antimicrobial effects and are effective on Helicobacter pylori bacteria (the cause of gastric and duodenal ulcers) **[58]**.

24. Gasterin

Product component: Each Gasterin tablet contains the following plant materials: Licorice root, flowering aerial parts of yarrow, Shiraz chamomile flowers.

Active ingredients: The main constituent of Gasterin tablets are: flavonoids glycosides such as: liquiritin, isoliquiritin, coumarin derivatives (herniarin), glycyrrhizin, glycyrrhetinic acid, alkaloid derivatives such as alekine, and volatile oils such as kamazolen **[59]**.

Pharmacological effects and mechanism of action: Acute and chronic gastritis are considered to be the most common complications of gastric mucosal inflammation. Plants existing in gasterin tablets have anti-inflammatory and anti-spasm effects. In addition, flavonoids and saponins in this plant stimulate and increase protective stomach mucus hypersecretion for gastric protection, and act as a protective barrier to prevent the effect of stomach acid on gastric ulcer **[60]**. Chamomile and yarrow in these products, especially with anti-inflammatory properties in peptic and duodenal ulcers, are very effective. Glycyrrhizin and aglycones acid glycerin are also two effective combination of licorice, which increases the secretion of gastric mucosa, and has an anti-heartburn effect. The antispasmodic effect of gastrin tablets is related to the flavonoids. The essential oils of chamomile and Shiraz yarrow have strong antibacterial effect, and are

ffective on Helicobacter pylori bacteria (the cause of gastric and duodenal ulcers) **[61, 62]**.

25. Galega

Active ingredients: Galega tablets contain 500 mg of Galega officinalis leafs (improved type). The chemical composition consists of saponins, flavonoids, and guanidinium derivatives (4-Hydroxy galegine, and galegine), and quinazoline alkaloids such as peganine.

Mechanism of action: This plant with the following mechanism reduces blood sugar: 1. strengthening the effect of insulin specially increasing glucose entry into cells. 2. Inhibiting glucose absorption in the intestine. 3. Inhibiting of gluconeogenesis (the biochemical process of making sugar in the body).

Medical properties and Uses: Galega plant has been used in Europe for many years to treat diabetes. The hypoglycemic effect of this plant is due to the presence of guanidinium in its leaves, which acts similar to synthetic guanidinium such as metformine. Due to its hypoglycemic effects and regulation of blood sugar in diabetic patients it prevents damage to the retina (Retionopathy) and kidney damage (Nephropathy). In addition, the composition of this plant causes the growth of the mammary glands and increases milk production and secretion **[63]**.

26. Licophar

Product component: Dried licorice extracts 51.2 mg, eucalyptus essence 1.07 mg, capsicum annum tincture 0.14 mg.

Active ingredients: The main active ingredient of licophar tablet is glycyrrhizin (6-10%). It is converted by intestinal bacteria to glycyrrhetinic acid. Other ingredients include flavonoids, isoflavonoids, and triterpenoid saponins.

Pharmacological effects and mechanism of action: Modern research has shown that glycyrrhizin has anti-allergic properties **[63]**. Active ingredient in licorice and eucalyptus essence have an anti-microbial effect on staphylococcus aureus, various species of streptococcus, and candida fungus. The antimicrobial effects of this plant are due to its isoflavonoid compounds **[64]**. The significant anti-inflammatory effects of glycyrrhetinic acid have been proven **[65]**. This herb has anti-viral properties, and it caused by the activation of interferon (a natural substance in the body) that causes a strong antiviral effect. Interferon causes cell surface connection, stimulates intracellular protein synthesis, and inhibits the viral DNA **[66]**. Licorice induces sputum and enhances respiratory mucus. This drug also relieves coughing. It is also recommended for hoarseness and tight throat **[67]**.

27. Livergol

Product component: Coated tablets contain granules dried fruit extract of Silybum marianum.

Active ingredients: Silybum marianum contains flavonolignans such as silybin, silicristin, silidianin, and their 2- and 3-dihydro derivatives. The flavonolignan group is called silymarin.

Pharmacological effects and mechanism of action: Human liver has several important vital actions such as digestion, metabolism, and detoxification of the body's waste, any type of liver damage may cause changes in liver cells and this will affect the power of liver function. Since free radicals are involved in lipid peroxidation in different types of liver toxicity, strong anti-oxidation effect of silymarin and silybin might justify their protective effects against various toxic agents of the liver. These two combinations act as destroyers of free radicals, and prevent high oxidative processes involved in Liver lesions induced by carbon tetrachloride, thallium, ethanol, paracetamol, and other liver toxic materials. Silymarin increases RNA polymerase enzyme activity in the cell nucleus and stimulates the synthesis of ribosomal proteins and this action increases the renewal power of liver cells. In addition to this, it acts as a direct antioxidant and removes toxic free radicals **[68]**. Silymarin is effective in treating both acute and chronic hepatitis virus. In a study on 29 patients with viral hepatitis treated with silymarin, it was showed that silymarin had a significant effect on the increased studied parameters, such as bilirubin levels in serum and liver enzymes, compared with the placebo group **[69]**.

28. Masument

Product component: Masument tablets contain 0.5% peppermint oil (Mentha Piperita) and 5% licorice extracts (Glycyrrhiza glabra).

Active ingredients: Peppermint contains essences, the most part of which consists of menthol and menthone. In addition, mint has a significant amount of tannins found in root of licorice, glycyrrhizin, and flavonoids **[70]**.

Pharmacological effects and mechanism of action: The menthol in peppermint in low concentrations selectively stimulates cold-related sensory nerve endings, thus causing the cold sensation. It also acts as an anti-irritant stimulation (counter-irritant) and an analgesic. Glycyrrhizin and glycyrrhetinic acid in licorice extract have anti-inflammatory and anti-allergic effects with a mechanism of action similar to corticosteroids. The volatile oils in peppermint oil have antispasmodic effects and reduce lower esophagus sphincter

tonus and facilitate the exiting of gases from the stomach **[71]**.

29. Moderic

Product component: Each tablet consists of 294-332 mg of dry aerial extract of horsetail plant

Active ingredients: it contains silicic acid minerals, silicates, potassium, aluminum, magnesium, flavonoids, and quercetin glycosides **[72]**.

Pharmacological effects and mechanism of action: Renal diseases such as glomerulonephritis and cystitis are considered major medical problems. In these patients the renal cell membranes are damaged and this damage might become more severe due to the effects of chemicals and their metabolites and cause urine dysfunction. To relieve urinary disorders, diuretic drugs are used. The clinical experimental evidences in Japan and China have proved that diuretic plants were effective **[73]**. Active ingredients of horsetail plant (flavonoids and saponins) have diuretic properties and accelerates the disposal of water and salt from the body **[74, 75]**. This plant has attracted attention in Europe and the U.S. due to its disinfection of the urinary tract and increasing the excretion of urine. Horsetail herb increases blood flow to the kidneys and this will increase the urinary excretion. Experimental studies have shown that horsetail plant has expels stones from the kidney, and that this plant has a mild effect in dissolving kidney stones. This effect is due to its potency in making the urine alkaline and due to its antiseptic activity. In addition to diuretic properties of horsetail herb, due to its silicic acid content, it strengthens the connective tissue and bones **[76]**.

30. Memorex

Product component: Memorex tablet contains 40 mg of standardized dried extract of temple tree leaves (Ginkgo biloba). Each tablet contains at least 9.6 mg flavone glycosides and 2.4 mg terpene lactones. Due to the harmful effects of ginkgolic acid in Ginkgo biloba, the extract used in Memorex tablets contains the least amount of this substance (less than 1 ppm) compared to similar products.

Pharmacological effects and mechanism of action: Flavonoids and ginkgolides are responsible for the pharmacological effects of the drug. Flavonoids in Ginkgo biloba plant cause neutralization or inactivation of toxic oxygen radicals. On the other hand, with increased release of catecholamines and other neurotransmitters and the reduction of disintegration of neurotransmitters, it increases their surface level within the nerve terminal and enhances the effects of these neurotransmitters. Furthermore, through

inhibition of the two catechol-O-methyltransferase (COMT), and monoamine oxidase (MAO) enzymes, they have a role in the treatment of neurological diseases, including depression and Parkinson's disease. The second group of compounds, ginkgolides, through antagonistic effect of the platelet aggregation factor (PFA), prevents clots in the body, and reduces risk of hypoxic damage to brain tissue in embolic and ischemic stroke. In addition, it is effective in slowing down the process of nerve damage in patients with degenerative diseases **[77]**.

31. Mentha

Active ingredients: Each Mentha tablet contains 5% mint leaves, and 0.5% of spearmint oil (Mentha Piperita). Mentha extract and its essence have a large amount of menthol and menthone and significant amounts of tannins **[78]**.

Pharmacological effects and mechanism of action: Menthol in peppermint in low concentrations stimulates cold-related sensory nerve endings, and causes cold sensation. The compounds existing in peppermint extract have spasmolytic, carminative, and antibacterial effect. In addition, by reducing lower esophagus sphincter tonus, it facilitates the exiting of gases from the stomach **[79]**.

32. Mentazin

Product component: Mentazin tablets contain 0.25% peppermint essence (Mentha piperita), 0.25% fennel essence (Feniculum vulgare), and 5% licorice extract (Glycyrrhiza glabra).

Active ingredients: Peppermint contains essences the most part of which consists of menthol and menthone. In addition, mint has a significant amount of tannins. In addition to the essence of fennel seed, most of it consists of anethole, and has various flavonoids. Licorice extract also contains glycyrrhetinic acid, steroidal saponins, and different flavonoids **[80]**.

Pharmacological effects and mechanism of action: Flavonoids and saponins of licorice, by increasing internal secretion, cause an increase in prostaglandin secretion in gastric mucosa, and have an important role in protecting the gastric mucosa, inhibiting gastric and duodenal ulcers, and in particular, inhibiting gastric acid secretion. The antispasmodic, analgesic, and carminative effects of licorice, due to the synergistic effect of volatile oil existing in peppermint and fennel essences, have significantly increased **[81]**.

33. Nervoxin

Active ingredients: Nervoxin tablet contains 400 mg of dry extract of hypericum (Hypericum perforatum) equivalent to 0.5 mg

Hypericin. In Hypericin compound extract the following ingredients exist: hypericin, pseudohypericin, and the flavonoids quercetin, and isoquercetin, rutin, and hypericin, and caffeic acid derivatives such as chlorogenic acid **[82]**.

Pharmacological effects and mechanism of action: According to studies, Hypericum extract and flavonoids have sedative, antidepressants, and anti-anxiety effects, and increase focus and comprehension. Studies on hypericin have shown that this matter, by inhibition of monoamine oxidase enzyme (MAO) and serotonin re-uptake, has antidepressants effects. Therapeutic doses of flavonoids in Hypericum, unlike synthetic antidepressant drugs, have no adverse effects and after its long term prescription, no dependency is observed after withdrawal. The therapeutic effect of Hypericum differs from antidepressant drugs of Psychogenic Somatogenic. Hypericum is commonly prescribed with low dosages; thus, its therapeutic effect will gradually become apparent. Moreover, 4 to 6 weeks is needed to achieve the desired effects of the drug. The most recent researches have shown that Hypericum extract can increase cellular oxygen uptake **[83]**.

34. Neurogol

Product component: Materials used in each tablet include the dry extract of: 160 mg of valerian root and 80 mg Melissa (leaf).

Active ingredients: 1-Valerian: alkaloids (containing actinidin, and valerianine), valepotriates (including valtrates, didrovaltrates, and isovaltrates, volatile oils (including bizabolen oil, varnole, and valerenic acid), 2-Melissa: volatile oils (including citral A and B, geraniol, linalool), flavonoids, luteolin 7-glucoside, rhamnazin, and polyphenolic compounds.

Pharmacological effects and mechanism of action: Experimental studies on animals have shown that valerian extract has a sedative effect. This effect is due to volatile oil and valepotriate compounds. It is also known that valerenal and valerenic acid are the strongest sedative compounds in valerian **[84]**. Documented biochemical studies have shown that valerenic acid inhibits the enzyme system responsible for the catabolism of GABA. The increasing concentration of GABA in the brain causes the sedative effect of this drug **[85]**. The sedative effect of valerian appears in both subjects with normal sleep and with insomnia. In a study that was conducted on 100 randomly selected patients for 2 weeks, it was showed that valerian was more effective in relieving anxiety symptoms compared to diazepam **[86, 87]**. Melissa eliminates anxiety

and depression. This effect is due to its volatile oil content. The combined effect of Valerian and Melissa causes lasting sedative effects. It relaxes patients under stress and pressure and provides a favorable sleep for them **[87]**.

35. Valiflor

Product component: Valiflor tablet contains 100 mg valerian root extract (Valeriana officinalis), and 30 mg passion flower (Passiflora incarnata).

Active ingredients: The active ingredients of Valiflor contain valepotriate compounds, valerenic acid, essence, various flavonoids, maltol , harman alkaloids, and etcetera **[88]**.

Pharmacological effects and mechanism of action: The extract of valerian root, by binding to GABA receptors, adenosine, barbiturat, and benzodiazepines, causes a sedative effect. Total aqueous and alcoholic extracts of this plant have tendency towards GABAA receptors. Nevertheless, the chemical composition of this area is not clear. Valtrates, especially didrovaltrate present in valerian extract, bond with peripheral receptors of barbiturates and benzodiazepines. Some studies have attributed the sedative properties of this plant to their high concentration of glutamine. Glutamine is able to cross the blood-brain barrier, be absorbed by nerve endings, and then metabolized to GABA. Passion flower extract contains alkaloids, flavonoids, maltone, and ethyl maltol, which is effective in anxiety and insomnia that is usually associated with agitation **[89]**.

Row	Product name	Dosage form	Laboratory	Therapeutic effect
1	Aphrodite	Coated tablets - Drop	Gol Daroo	Resolves disorders of sexual abilities
2	Agnugol	Coated tablets	Gol Daroo	Relieves menstrual problems and menopause
3	Althadin	Chewable tablets	Dineh Iran	Anti-inflammation of the lining of the throat and mouth
4	Alicom	Coated tablets	Niak	Lowering blood pressure, lipid-lowering
5	Allium-S	Coated tablets	Dineh Iran	Lowering blood pressure, lipid-lowering
6	Echiherb	Tablets	Gol Daroo	Stimulation of the immune system
7	Perforan	Coated tablets	Gol Daroo	Antidepressants, sedatives, anti-migraine
8	Prostatan	Coated tablets - Drop	Gol Daroo	Effective in the treatment of prostatic hyperplasia
9	Tabokan	Tablets	Niak	Disorders resulting from organic brain syndrome
10	Ginkgo T.D	Tablets	Toulid Darou	Relieve symptoms of organic brain disorders
11	Ginkogol	Coated tablets	Gol Daroo	Relieve symptoms of organic brain disorders
12	Rasin	Chewable tablets	Ebn Masouyeh	Carminative - smooth throat
13	Salvigol	Tablets	Gol Daroo	Reduction of body sweating
14	Samilax	Tablets	Samisaz	Laxatives, stimulant, laxative
15	Sena-Lax	Tablets	Iran Darook	Laxatives, stimulant, laxative
16	C-Lax	Tablets	Dineh Iran	Laxatives, stimulant, laxative
17	Cynarchol	Tablets	Dineh Iran	Increases secretion of bile
18	Cynaroll	Tablets	Niak	Increases secretion of bile
19	Chicoridin	Tablets	Dineh Iran	Appetizing- tonic

20	**Phytocold**	**Coated tablets**	**Gol Daroo**	**Treatment of cold symptoms**
21	**Cratagol**	**Coated tablets**	**Gol Daroo**	**Heart failure type 2**
22	**Garcin**	**Coated tablets**	**Gol Daroo**	**Lowering blood pressure, lowering blood fat**
23	**Gasterodin**	**Tablets**	**Dineh Iran**	**Gastrointestinal inflammation**
24	**Gasterin**	**Tablets**	**Gol Daroo**	**Anti-inflammatory and stomach pain reliever**
25	**Galega**	**Tablets**	**Dineh Iran**	**Hypoglycemic**
26	**Licophar**	**Chewable tablets**	**Gol Daroo**	**anti-inflammatory, anti-cough**
27	**Livergol**	**Coated tablets 70 and 140 mg**	**Gol Daroo**	**Adjuvant treatment of liver toxicity**
28	**Masument**	**Chewable tablets**	**Ebn Masouyeh**	**Carminative, smooth throat**
29	**Moderic**	**Coated tablets**	**Gol Daroo**	**Urinary tract antiseptic**
30	**Memorex**	**Tablets**	**Iran Darook**	**Treatment of cerebral blood flow restriction**
31	**Mentha**	**Chewable tablets**	**Dineh Iran**	**Carminative, digestive antispasmodic**
32	**Mentazin**	**Chewable tablets**	**Ebn Masouyeh**	**Carminative, smooth throat**
33	**Nervoxin**	**Tablets**	**Dineh Iran**	**Antidepressants, sedatives**
34	**Neurogol**	**Coated tablets**	**Gol Daroo**	**Sedative-hypnotic**
35	**Valiflor**	**Coated tablets**	**Niak**	**Hypnotic**

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