

DIARRHEA AND SOME EFFECTIVE MEDICINAL PLANTS FOR ITS TREATMENT

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RESUME

Diarrhea refers to the frequent (more than 3 times daily) passage of a *liquid* or *semiliquid* stool. It may be acute or chronic. Symptomatic measures are used for brief episodes of acute diarrhea and for chronic diarrhea, causal treatment of the underlying disease is essential.

Common causes of diarrhea are bacterial and viral infections, food intolerance, parasites, reactions to medicines, intestinal diseases.

Phytomedicines have a significant role, both as traditional home remedies and as galenic preparations, in the symptomatic treatment of diarrhea. Three groups of preparations are particularly important: tannin-containing herbs, pectins, and a special strain of live dried yeast.

Tannins have a protein-precipitation action. In the intestinal tract tannins line the bowel lumen with a protective film that hamper the absorption of toxins, blunt the action of local irritants and normalize hyperperistalsis. To some effective antidiarrheal tannin containing plants are *Camelia sinensis*, *Vaccinium myrtillus*, *Potentilla erecta*, and *Quercus robur*. Pectins, another antidiarrheal remedies, are biopolymers that have the ability to hold water and form gels. In the small intestine, pectin gels can form a protective film on the mucosa.

The antidiarrheal action of yeasts depends on its antagonist effects on pathogenic microorganisms and its stimulatory effects on the immune system. The tropical wild yeast, *Saccharomyces cerevisiae*, known internationally as *S. Boulardii*, was discovered by the French mycologist Henri Boulard in 1923 while travelling in Indochina. This yeast is one of the most effective remedies against acute diarrhea.

The following article summarizes data on some medicinal plants that have successfully been used by folk medicines for centuries and that have been scientifically proved to be very effective in the treatment of acute diarrhea.

Key words: diarrhea, pectins, *Camelia sinensis*, *Vaccinium myrtillus*, *Potentilla erecta*, *Quercus robur*, *Saccharomyces cerevisiae*.

დიარეა და მის სამკურნალოდ გამოყენებული ზოგიერთი ეფექტური სამკურნალო მცენარე

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რეზიუმე

დიარეა არის მდგომარეობა, როცა კუჭის მოქმედების რაოდენობა ერთ დღეში სამზე მეტია და განავალი არის თხევადი ან ნახევრად თხევადი. დიარეა შესაძლოა იყოს მწვავე ან ქრონიკული. მწვავე დიარეის მკურნალობა შესაძლებელია სიმპტომურად, ხოლო ქრონიკული დიარეისას, მისი გამომწვევი დაავადების მკურნალობა არის აუცილებელი.

დიარეის გამომწვევი მიზეზი შეიძლება იყოს ბაქტერიული ან ვირუსული ინფექცია, საკვებით მოწამლა, პარაზიტები, მედიკამენტის გვერდითი მოვლენა, ნაწლავური დაავადება.

დიარეის სიმპტომური მკურნალობაში მნიშვნელოვანი ადგილი უჭირავთ ფიტოპრეპარატებს, როგორც ოჯახური საშუალებების, ისე გალენური პრეპარატების სახით. მნიშვნელოვანია სამი ტიპის პრეპარატები: ტანინის შემცველები, პექტინები და მშრალი საფუარის განსაკუთრებული შტამი.

ტანინს გააჩნია ცილის დამლექავი თვისება. ცილა ილექება ეპითელიუმის ზედაპირზე და წარმოიქმნება დამცავი გარსი. წვრილ ნაწლავში დამცავი გარსი გადაეკვრება შიდა კედელს, რითაც ხელს უშლის ტოქსინების აბსორბციას, ამცირებს გამღიზიანებლების მოქმედებას, არეგულირებს პერისტალტიკას. ეფექტურ დიარეის სამკურნალო მცენარეებს

მიეკუთვნება *Camelia sinensis*, *Vaccinium myrtillus*, *Potentilla erecta*, and *Quercus robur*.

პექტინები ბიოპოლიმერებია, რომელთაც გააჩნიათ წყლის შეკავების და გელის წარმოქმნის უნარი. მცირე ნაწილში პექტინის გელი წარმოქმნის ლორწოვანი გარსის დამცავ ფენას.

საფუარის დიარეის სამკურნალო თვისება ეფუძნება პათოგენურ მიკროორგანიზმებზე მის ანტაგონისტურ მოქმედებას, იგი ასევე წარმოადგენს იმუნური სისტემის მასტიმულირებელ საშუალებას. ტროპიკული სფუარი *Saccharomyces cerevisiae*, რომელიც საყოველთაოდ ცნობილია, როგორც *S. Boulardii*, აღმოაჩინა ფრანგმა მეცნიერმა ჰენრი ბულარდმა 1923 წელს ინდოჩინეთში მოგზაურობისას.

წინამდებარე სტატიაში თავმოყრილია მონაცემები ზოგიერთ სამკურნალო მცენარეზე, რომლებიც საუკუნეების განმავლობაში გამოიყენებოდა ხალხურ მედიცინაში, ხოლო მეცნიერულმა შესწავლამ დაადასტურა მათი ეფექტურობა დიარეის სამკურნალოდ.

საკვანძო სიტყვები: ფალარათი, პექტინები, *Camelia sinensis*, *Vaccinium myrtillus*, *Potentilla erecta*, *Quercus robur*, *Saccharomyces cerevisiae*

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Diarrhea refers to the frequent (more than 3 times daily) passage of a *liquid or semiliquid stool*. (2)

Diarrhea may be accompanied by cramping pain, bloating, nausea, or an urgent need to use the bathroom. Fever or bloody stools may also be present. Diarrhea is potentially dangerous in newborns and infants, as it can lead to dehydration. General signs of dehydration include thirst, less frequent urination, dry skin, fatigue, and light-headedness. Signs in children are dry mouth and tongue, absence of tears when crying, dry diapers for three hours or more, high fever, listlessness or irritability, skin that does not flatten when pinched and released, and sunken abdomen, eyes, or cheeks.

Diarrhea is an important symptom that can have many causes. These range from intestinal infection and food sensitivities to colitis and anxiety. Prolonged diarrhea can be a sign of other problems. It can also cause dehydration, a condition in which the body lacks adequate fluid to function properly (3).

Diarrhea may be acute, persistent, or chronic. Acute Diarrhea has an abrupt onset, usually lasts 3-4 days, often has an infectious cause and tends to be self-limiting. Persistent diarrhea lasts longer than 2 weeks and less than 4 weeks.

Chronic diarrhea persists longer than 4 weeks and may be symptomatic of a chronic underlying illness such as ulcerative colitis, Crohn's disease, or hyperthyroidism (1).

A few of the more common causes of diarrhea are the following:

1. Bacterial infections caused by consumption of contaminated food or water; common culprits include *Campylobacter*, *Salmonella*, *Shigella*, and *Escherichia coli*.
2. Viral infections, including rotavirus, Norwalk virus, cytomegalovirus, herpes simplex virus, and viral hepatitis.
3. Food intolerance, such as intolerance of lactose, the sugar, found in milk
4. Parasites, including *Giardia*, *Entamoeba*, and *Cryptosporidium*
5. Reactions to medicines, including antibiotics, antihypertensives, and antacids containing magnesium
6. Intestinal diseases, such as inflammatory bowel disease
7. Functional bowel disorders, for examples, irritable bowel syndrome, in which the intestines do not work properly.

Symptomatic measures are used for brief episodes of acute diarrhea that may be both dietary and pharmacologic. As for chronic diarrhea, causal treatment of the underlying disease is essential.

The fluid and electrolytes (especially potassium and sodium) lost during diarrhea must be replaced, as the body cannot function properly without them. Water is essential to prevent dehydration, but it does not contain electrolytes. To maintain electrolyte levels, the patient must be given chicken or beef broth, which contains sodium and fruit beverages, which contain potassium. For children a rehydration solution that contains these necessary nutrients, must be used.

In most cases, replacing lost fluid to prevent dehydration is the only treatment necessary for diarrhea. Medicines that stop diarrhea may be helpful in some cases, but they are not recommended for people with diarrhea caused by bacteria or parasites, as stopping the diarrhea will trap the organism in the intestine and prolong the problem.

Until diarrhea subsides, milk products and foods that are greasy, high in fiber, or very sweet must be avoided, as they tend to aggravate diarrhea. As the condition improves, soft, bland foods, such as bananas, plain rice, boiled potatoes, toast, crackers, cooked carrots, and baked chicken with no skin or fat may be added to the diet. For children, BRAT diet (Bananas, rice, applesauce, and toast) is recommended (3).

Phytomedicines have a significant role, both as traditional home remedies and as galenic preparations, in the symptomatic treatment of diarrhea. Three groups of preparations are particularly important: tannin-containing herbs, pectins, and a special strain of live dried yeast.

Tannin Containing Herbs	Pectins	Aspecial strain of live dried yeast
• Green tea • Black tea • Bilberries • Tormentil Rhizomes • Oak Bark	• Pectins	• Saccharomyces cerevisiae – S. Boulardii

Tannins are polyphenolic compounds

($C_6 - C_3 - C_6$)_n that precipitate proteins and form complexes with polysaccharides, and are composed of a very divers group of oligomers and polymers.

The phytochemical classification of tannins can be complex, but two main groups are usually recognized: condensed (the procyanidins or proanthocyanidins) and hydrolyzable tannins. Hydrolysable tannins usually consist of a central glucose molecule linked to molecules of gallic acid (gallotannins) or hexahydroxydiphenic acid (ellagitannins). They are readily hydrolyzed, hence their name. Ellagitannins are found in herbs such as pomegranate, cranesbill, oak bark and meadowsweet.

Hydrolysable and condensed tannins are unevenly distributed in plants. The condensed tannins occur almost universally in ferns and gymnosperms and are widespread among angiosperms, especially trees and shubs. By contrast, hydrolyzable tannins are limited to dicotyledonous plants Both types of tannin can occur together in the same plants. E.g. Oak Bark (*Quercus robur*) also contains both types of tannins (3)

Tannins have a protein-precipitation action. They cause proteins to be deposited on the epithelial surface forming a stable membrane. In the intestinal tract tannins line the bowel lumen with a protective film that hamper the absorption of toxins, blunt the action of local irritants and normalize hyperperistalsis (2).

Tannins can provide short-term healing anti-inflammatory effects on the gut wall, though likely to rapidly reduce transit through the tract unless in slowly dispersing solid form. Effects on the bowel during diarrhea can be significant if the symptom is a reflex consequence of irritation in the gastric or upper enteric passages (gastroenteritis). The use of tannins is not to be recommended as a long-term solution (3).

The first representative of tannin-containing herbs used in treatment of diarrhea is the tea shrub (*Camellia Sinensis*, formerly known as *Thea sinensis*). *Camellia Sinensis* is an evergreen woody plant that is native predominantly to southeast Asia and can grow to 5 m. The cultivated plant is pruned to a bushy shrub to facilitate harvesting. The leaves are harvested and dried to yield the crude drug (11).

For manufacturing green tea, *Camellia Sinensis* freshly harvested leaves are heated immediately, before drying, mechanically rolled and crushed to avoid enzy-

matic changes. Stemmed from this, green tea is particularly rich in tannins and is strongly astringent.



Figure1. *Camellia Sinensis* flower



Figure 2. *Camellia Sinensis* shrubs

Just the opposite actions are taken to produce black tea. The harvested leaves are left in humid environment for several hours to promote enzymatic changes. As a result, leaves gradually turn into reddish brown and acquire pleasant aroma(6).

The polyphenolics in green tea (*Camellia sinensis*) are a class of pseudotannins known as catechins. These are

smaller molecules than tannins. While they do possess some astringency, they cannot tan hides, although they have been classified as condensed tannins in some publications. Green tea also contains condensed and hydrolysable tannins (15).

Twelve healthy individuals were involved to test *Camellia Sinensis* infusion impact on resolving diarrhea. The test subjects were consuming 2 litre of tea infusion daily (contained 8 g of herb). The result showed that after 4 days of consumption, intestinal transit time was significantly prolonged comparing to placebo group.

However, tannins become hepatotoxic if tea were consumed to excess by the individual with preexisting liver damage. E.G. one woman consuming 65 g tea per day for 5 years developed liver dysfunction. But problems resolved after tea was withdrawn. When proper attention is given to the caffeine content of tea, the usage risk is minimal (4).

Bilberries (European blueberries) are dried ripe fruit of *Vaccinium myrtillus*, a dwarf shrub of a family *Ericaceae*.

It is a small shrub, approximately 30 to 40 cm high with erect, branched flowering stems. The alternate, light green leaves are flat, oval and pointed with a toothed margin; Flowers contain four to five white or pink petals. The fruit is deep violet, fleshy berry enclosing crescent-shaped seeds (12).

The *Vaccinium* genus contains hundreds of species, many with edible berry-like fruits (Including the American cranberry, *V. macrocarpon*). Bilberry fruit is well known as a food, and in particular as a jam. The name derives from a Danish word meaning dark berry, because unlike the blueberry, its pulp as well as skin is dark blue. Bilberry has been used in Europe to color wine and to dye wool. During World War II, bilberry jam or wine was consumed by RAF pilots to improve their night vision. It is available as fresh or dried fruit, fluid extract or in solid dose form as a tablet or capsule.



Figure 3. *Vaccinium myrtillus* fruits

Traditionally Bilberry fruit was used to treat diarrhea, dysentery, gastrointestinal inflammation, haemorrhoids

and vaginal discharges and to "dry up" breast milk. It has also been used to treat scurvy and for urinary complaints (3).

Dried Bilberries contain: 5-10% catechins, about 30% invertose and small amount of flavonone glycosides and anthocyanosides, particularly, glycosides of malvidine, cyaniding, and delphinidin. 20-60 g of dried berries are soaked in water or red wine, then chewed well and swallowed (daily dose). Alternatively, it can be consumed fresh in amount of 5-10 times the quantity of dried herb. Bilberries are particularly recommended in school age children (2)

The dosage is 3 to 6 ml of 1:1 fluid extract per day. Tablets of capsules contain dried extracts of the fresh berries that deliver 60 to 160 mg or more of anthocyanins per day (equivalent to about 20 to 60 g of fresh fruit). The dose may be taken long term for most applications.

High doses (more than 100 mg/day anthocyanins) should be used cautiously in patients with haemorrhagic disorders and in those taking warfarin or antiplatelet drugs, because of the observed human antiplatelet activity.

Concentrated bilberry powder in a study of infants with acute dyspepsia was well tolerated (3).

As an antidiarrheal, bilberries were used in combination with other herbs in Georgian folk medicine. The receipt is as follows: 5 g of bilberries, 5g of peppermint, and 7.5 g of chamomile are added 700 ml of boiled water, cooled, strained and taken 100 ml 3-4 times a day (20).

The dried rhizome of Tormentil (*Potentilla erecta*) is another antidiarrheal plant. The plant is also known as cinquefoil or potentilla. It is a herbaceous plant of the family *Rosaceae*, *Potentilla erecta* is a low, clump-forming plant with slender, procumbent to arcuately upright stalks, growing 10-30 centimetres tall. It grows wild predominantly in Europe, Western Asia and North America, mostly on acid soils and in a wide variety of habitats such as mountains, heaths, meadows, sandy soils and dunes. The rhizomatous root is thick. It has little value for food use because of its bitterness and low caloric value. The plant is used in herbal medicine as an astringent because of its tannin content, which is unusually high for a herbaceous plant. The crude drug is odorless and has a strongly astringent taste. The herb contains catechins (15-20%) and tannins (1-2%) (7).

Roots from the genus *Potentilla* typically contain hydrolysable and condensed tannins (13). In a randomised, double blind, placebo-controlled trial, an extract of tormentil root (*Potentilla erecta*) effectively treated rotavirus infection in children (14). The duration of diarrhea in the herbal group was 3 days, com-

pared with 5 days in the control group ($p < 0.0001$).

It is used as a tea – 2-3 g herb in 1 cup of water 150 ml. The Recommended dose for acute nonspecific diarrhea is 1 cup 2-3 times daily between meals. Another receipt for the tincture is as follows: 20 g finely chopped rhizomes are steeped in 200 ml 70 % ethanol, periodically stirred and finally, strained after 10-12 days. 30-40 drops of the tincture is diluted by water and taken 3-4 times a day (19). Side effected may include nausea and vomiting (14).



Figure 4. Potentilla erecta



Figure 5. Potentilla erecta rhizome

Quercus species, also known as oak, represent an important genus of the Fagaceae family. It is widely distributed in temperate forests of the northern hemisphere and tropical climatic areas. Dried bark of young twigs of *Quercus robur* is harvested in spring. It is the bark from several types of oak trees.

Many of its members have been used in traditional medicine to treat and prevent various human disorders such as asthma, hemorrhoid, diarrhea, gastric ulcers, and wound healing (17). All mentioned effects are attributed to the specific chemical composition, com-

prised mainly of triterpenoids, flavonoids, and tannins.

Dried bark of foak tree contains 1-20% condensed tannins, including high content of gallotannins, 13-14% of pentosanes, 6 % pectins, quercetin and carbohydrates. Because of tannins, it has astringent and antiviral properties.

Antidiarrheal effect of oak bars was described in old Georgian, Polish Bulgarian medicinal books (19).



Figure 6. Oak tree



Figure 7. Quercus robur

Up to three grams (3/4 teaspoon) of dried oak bark is boiled in a few cups of water, strained, and drunk two table spoons 2-3 times a day. Because of high content of tannins, should not be taken more than 3-4 days (16). Another receipt is preparation of macerate - 5 g finely chopped oak bark is steeped in 400 ml cold water for 8 hours and the extract taken in one day (children must not be given this macerate) (19). It can be used externally for mild inflammatory conditions involving mouth, throat, genitalia or anal region. Oak bark can inhibit trace elements and B vitamin absorption. There-

fore, it should not be given to the patient in high doses for long periods, or alternatively given from food and other medications (3).

Pectins are biopolymers with molecular weight of 60 000 to 90 000. Their basic structural framework is formed by galacturonic acid molecules. Numerous acid groups give pectins their ability to hold water and form gels. These gels are not attacked by digestive enzymes and pass unchanged into the colon, where they are broken down by colonic bacteria. In the small intestine, pectin gels can form a protective film on the mucosa.

One hypothesis is that the short-chain fatty acids released from the microbial breakdown of pectins in the colon have an inhibitory action on colonic motility.

Pectins consistently accompany cellulose, so they contribute much to the structural integrity of the cell. They are present to some degree in all plant products but are particularly abundant in fleshy fruits and storage roots. Rich commercial sources are sugar beet gragments, apple residue, orange and lemon waste product and carrots.



Figure 8. Apple pectin

The following “home remedies” dietary constituents have proven useful in the treatment of diarrhea:

1. 1-1.5 kg of raw greated apples, eaten throughout the day;
2. Bananas, cut into small pieces and eaten as often as desired (recommended for children)
3. Carrot preparations are suitable for infants and small children, e.g. 500 g of peeled carrots are boiled in 1 litre of water for 1-2 h, poured through a strainer, and pureed in a blender. Water is added to make 1 litre, and 3 g table salt is added (18).

Travelling through Indochina in 1923, the French

mycologist Henri Boulard noticed that the native population used the skins of tropical fruits as a remedy for diarrheas. A yeast isolated from the surface of these fruits had antidiarrheal properties This tropical wild yeast is *Saccharomyces cerevisiae*, known internationally as *S. Boulardii*.



Figure 9. *Saccharomyces cerevisiae*

Yeasts occur ubiquitously in nature wherever there are fermentable juices with a high sugar content

Unlike bacteria, yeast have a true cell nucleus and are classified as fungi. This makes *S. Boulardii* a member of the plant kingdom, so its medicinal use is a form of phytotherapy

The antidiarrheal action depends on its antagonist effects on pathogenic microorganisms and its stimulatory effects on the immune system. Its therapeutic efficacy depends on the viability of the yeast cells, which must be sustained as the cells pass through the intestinal tract. On entering the colon, however, the cells undergo a bacterial breakdown that leaves only 0.05 % of the ingested dose of yeast cells to be excreted in the stool.

S. Boulardii is antagonist to a number of pathogenic microorganisms which are damaged or destroyed by the presence of the cells

E. g. mannose structures on the surface of the cells enable them to bind and entrap pathogenic *E. coli*. *S. boulardii* can also reduce the activity of bacterial toxins.

According to scientific researches conducted, it has been stated that *S. boulardii* is effective to prevent:

Nutritionally related diarrhea in patients fed by gavage, travel-related diarrhea, antibiotic-associated diarrhea, Crohn's disease.

Recommended dose is 250-500 mg/day, with a daily does of 500 mg recommened for diarrhea related to feeding by gavage.

For the prevention of travel-related diarrhea, treatment should be initiated 5 days before the start of the trip

In cases of acute diarrhea, treatment should be continued for several days after symptoms have abated

There have been reports of bloating and sporadic intolerance reactions in the form of itching, urticaria, and generalized skin eruptions. Yeast sensitivity is a contraindication. A fall in blood pressure may occur as a drug interaction in patients who are also taking a monoamine oxidase inhibitor.

Having studied and analysed the scientific and historical data on the above mentioned medicinal plants, we concluded that for centuries, number of medicinal plants have been used in folk medicine for treatment of acute diarrhea with significantly less side effects. These well tested receipts have to be restored and consumed together with popular widely used synthesized medications.

REFERENCES:

1. David Hoffmann. Medical Herbalism. The Science and practice of herbal medicine. Healing Arts Press, Rochester, Vermont. 2003, pp. 264-266
2. Schulz V., Hansel R., Blumenthal M., Tyler V.E. Rational Phytotherapy. Fifth edition. Springer, Berlin, Heidelberg, New York. 2003. pp. 257-265.
3. Bone, Kerry. Mills, Simon. Principles and practice of phytotherapy. Modern herbal medicine-2nd ed. 2013, pp. 104, 191,
4. Hojgaard I., Arffmann S., Jorgenson M., Krag E. Tea consumption: a cause of constipation. Br Med J pp. 282-284.
5. Jahn HU, Zeit M (1991). Immunmodulatorische Wirkung von *Saccharomyces boulardii* beim Menschen. In: Seifert J, Ottenhann R, Zaitz M, Brockenmuhl J (eds) Darm III. Springer Verlag, pp. 159-164.
6. Ludewig R (1995) Schwarzer und Gruner Tee als Genus und Heilmittel. Dtsch Apoth Z 135, pp. 2203-2218
7. Lund K, Rimpler H (1985). Tormentillwurzel. Dtsch Apoth Z 125, pp. 1105-1107.
8. Massot J, Desconclois M, Atoin J (1982). Protection par *Saccharomyces boulardii* de la diarrhée à *Escherichia coli* du souriceau. Ann Pharm Fr 40. Pp. 445-449.
9. Plein K, Hotz J. (1993). Therapeutic effect of *Saccharomyces boulardii* on mild residual symptoms in a stable phase of Crohn's disease with special reference to chronic diarrhea – a pilot study. Z. Gastroenterol 31: pp. 129-134.
10. Schmitz B, El Agamy R, Lindner K (1992). Uzarawurzel – seit 80 Jahren bewahrt bei akuten Durchfallerkrankungen. Pharmazeutische Zeitung 137. Pp. 1697-1713.
11. Scholze, Bertram B (1995). *Camelia sinensis* (L.). O. Kuntze. Der Teestrauch. Z. Phytother 17. Pp. 235-250.
12. Chiej R. The Macdonald Encyclopedia of Medicinal Plants. London. Macdonald, 1984. P. 321.
13. Tomczyk M, Latté KP. Potentilla – a review of its phytochemical and pharmacological profile. J Ethnopharmacol. 2009;122(2)pp. 184–204.
14. Subbotina MD, Timchenko VN, Vorobyov MM, et al. Effect of oral administration of tormentil root extract (*Potentilla tormentilla*) on rotavirus diarrhea in children: a randomized, double blind, controlled trial. Pediatr Infect Dis J. 2003;22(8):706–711.
15. Nonaka GI, Sakai R, Nishioka T. Hydrolysable tannins and proanthocyanidins from green tea. Phytochemistry. 1984;23(8)pp. 1753–1755.
16. Blumenthal M., Hall T, Goldberf A. (eds.) (2003). The ABC Clinical Guide to Herbs. Austin, Tex: American Botanical Council.
17. Mehdi Taib, Yassine Rezzak, Lahboub Bouyazza, Badiaa Lyoussi. Medicinal Uses, Phytochemistry, and Pharmacological Activities of *Quercus* Species. Published online 2020 Jul 31. Doi:10.1155/2020.1920683. PMID:32802116.
18. Schulte FJ, Spranger J (1988). Lehrbuch der Kinderheilkunde. Fischer, Stuttgart, p. 320.
19. Iosebidge N., Wildgrown and cultivated healing plants in Georgia. Palitra L, 2022, pp. 193-195, 161-163.
20. Mamatsashvili T., 2000 herbal receipts. Palitra L. 2007. P-145.