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1. Abdullayeva U.K., Rakhimova M.B.	
Pomegranate seed oil for ulcerative colitis.....	7
2. Abdurakhmonova Q., Rakhimbaeva G.	
Inflammatory biomarkers and insulin resistance in acute ischemic stroke of different etiologies...	12
3. Boymuradov Sh.A., Khatamov U.A.	
Biomechanical and clinical analysis of atypical counterforces in maxillofacial trauma from electromechanical impacts.....	19
4. Baymuratova A.Ch.	
Tizza bo'g'imi ichki strukturalari jarohatlanishlarini utt orqali klinik baholash va fizioterapevtik reabilitatsiyani optimallashtirish	26
5. Boboyev Sh.R., Saidov G.N., Keldiyorova Z.D.	
Tajribaviy oshqozon-ichak traktining sirka kislotasi bilan kimyoviy kuyishida yo'g'on ichak devoridagi morfologik o'zgarishlarning qiyosiy tavsifi.....	32
6. Jumaeva G.A.	
Klinik farmakologiyada innovatsion o'quv modeli: talaba markazli yondashuv.....	38
7. Keldiyorova Z.D., Zaripova S.O.	
O'tkir respirator virusli infeksiyalar va torch- infeksiyasi bilan kasallangan bolalarda klinik-laborator o'zgarishlar.....	43
8. Khalikova F.Sh.	
Morphological structure of the thyroid gland of white rats in chemotherapy of breast cancer.....	51
9. Mirzayeva M.R., Yodgorova M.Sh.	
Latent course of liver fibrosis in patients with chronic hepatitis B: comparative evaluation of noninvasive diagnostic methods (APRI, FIB-4 and fibroscan).....	58
10. Muradimova A.R., Madjidova Y.N., Khidoyatova D.N., Sharipov F.R.	
Bioacoustic correction of cognitive impairment in stroke patients.....	69
11. Najmutdinova D.Q., Ismoilova Sh.S.	
2-tur natriy-glyukoza kotransportyori ingibitorlarini qo'llashda jigar fibroz ko'rsatkichlari va insulinga rezistentlik dinamikasi.....	74
12. Nazirxujayev F.A.	
Farg'ona viloyati aholisi orasida "O'rta yer dengizi parxezi"ni qo'llash orqali surunkali pankreatit xurujlari profilaktikasini optimallashtirish.....	79
13. Nurmatova O.A.	
Bolalarda nefrotik sindromning profilaktikasini takomillashtirish yo'llari (Farg'ona viloyati misolida).....	84
14. Ortiqboev J.O.	
Molecular genetic analysis of the renin–angiotensin system in chronic kidney disease.....	89

15. Oxunova M.J.	
Farg'ona viloyatida 3 yoshgacha bolalarda pnevmoniya rivojlanishiga ta'sir etuvchi asosiy xavf omillari.....	95
16. Rasulova N.R. Temirova N.R.	
Tajribaviy kimyoterapiya natijasida ayrisimon bezdagi morfologik o'zgarishlarning qiyosiy tahlili.....	99
17. Raxmatullayeva G.K., Axmedova N.A., Kasimova M.B., Xudayberganova N.X.	
Oshqozon-ichak kasalliklarida so'rovnomaga o'tkazish va uni o'rganish.....	108
18. Subkhanova Z.S., Raimkulova N.R.	
Interrelationship between gastroesophageal reflux disease and respiratory diseases: general pathogenetic mechanisms and modern research findings.....	112
19. Subxanova Z.S., Raimkulova N.R.	
Gastroezofageal reflyuks kasalligi, surunkali obstruktiv o'pka kasalligi va bronxial astma: komorbidlikning dolzarb masalalari.....	115
20. Temirova M.B., Kasimova M.B., Axmedova N.A.	
Metabolik assotsirlangan jigar yog' kasalligida bemorlarning tana tuzilishini bioimpedance spektroskopiya yordamida baholash.....	118
21. Tukhtaeva N.Kh., Musayev H.N.	
Development of gastropathy against the background of nonsteroidal anti-inflammatory drugs in patients with rheumatoid arthritis against the background of virulent genes of helicobacter pylori.....	123
22. Абдуллаева У.К., Рахимова М.Б.	
Ярали колит хавф омиллари: замонавий қарашлар.....	128
23. Абдулхаков И.У., Абдулхаков М.И.	
Общеврачебная практика как эффективная модель профилактики неинфекционных заболеваний.....	132
24. Адизова С.Р., Носирова З.Ж.	
Преэклампсия оғирлашувида гемостаз тизимининг таъсири.....	143
25. Акрамов О.З., Аблязов О.В., Кадыров Ш.У.	
Инновационные подходы нейровизуализации при опухолях функционально важных участков мозга у детей.....	149
26. Аликулова Н.А., Ўринова Г.М.	
Мия инфаркти ва СМИ ўтказган беморларда клиник-функционал кўрсаткичлар динамикаси.....	156
27. Алимов А.А., Алимов А.В., Шарипов А.М., Шоикрамов Ш.Ш.	
Профиль инотропной поддержки у детей после коррекции врождённых пороков сердца: частота, дозы и динамика применения.....	166
28. Аллокулов Р.Р., Акрамов В.Р., Нуралиев Ф.Н.	
Кекса ва қари ёшдаги шахсларда гонартрознинг клиник-иммунологик жиҳатлари.....	172

29. Асадов Х.Ф.

Хирургия мигрени: сравнительный анализ двух хирургических методик лечения височной мигрени: нейроэктомия и декомпрессия ветви скуловисочного нерва.....182

30. Аскарров Ш.Ш., Салахитдинов Ш.Н.

Перспективные интервенционные технологии при тромботических осложнениях острого коронарного синдрома.....187

31. Гадаев А., Халимова Х., Гадаева Н.

Ўпканинг сурункали обструктив касаллиги ва артериал гипертензияда буйраклар дисфункцияси (адабиётлар шархи).....193

32. Гаффорова В.Ф., Ходжиева Д.Т.

Клинико-нейрофизиологические характеристики фебрильных судорог у детей.....200

33. Давлетова Ш.Б.

Роль микробиоты кишечника в развитии неврологических заболеваний у детей.....205

34. Даминов Б.Т., Ортикбоев Ж.О.

Уровень витаминов группы В и витамина Д у больных с хронической болезнью почек в зависимости от прогрессирования заболевания.....216

35. Джураев И.Б., Курбанов О.М., Бабаназаров У.Т.

Клинические проявления патологий желудка у больных в критическом состоянии в условиях искусственного дыхания.....221

36. Жалалова В.З.

Оптимизация восстановительных процессов при физических нагрузках с помощью спирулины: морфофункциональные и клинические аспекты.....229

37. Ибодуллаева Н.М.

Бачадон саратон олди касалликлари бўлган аёлларда неврологик ва психоэмоционал ўзгаришларнинг психосоматик жиҳатлари.....237

38. Иноятов А.Ш., Ражаматов Т.Р., Умаров Б.Я.

Функциональная и иммунологическая обоснованность применения щечного жирового лоскута при палатопластике в детском возрасте.....241

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¹<https://orcid.org/0000-0002-1495-3668>²<https://orcid.org/0009-0009-7697-5369>**POMEGRANATE SEED OIL FOR ULCERATIVE COLITIS**
 <http://dx.doi.org/10.5281/zenodo.17352414>
ANNOTATION

Pomegranate seed oil consists of a complex set of fatty acids, approximately 80% of which are 18-carbon molecules with three alternating double bonds. In animal experiments, pomegranate seed oil has antioxidant, antitumor, and anti-inflammatory activity. The aim of our study is to increase the effectiveness of the treatment of ulcerative colitis, made in the form of rectal suppositories made from pomegranate seed oil.

Key words: ulcerative colitis, treatment, pomegranate seed oil, rectal suppositories.

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МАСЛА ГРАНАТОВЫХ КОСТОЧЕК ПРИ ЯЗВЕННОМ КОЛИТЕ**АННОТАЦИЯ**

Масло семян граната состоит из сложного набора жирных кислот, приблизительно 80% из которых составляют 18-углеродные молекулы с тремя чередующимися двойными связями. В экспериментах на животных у масла семян граната выявлены антиоксидантная, противоопухолевая, противовоспалительная активности. Целью нашего исследования повышение эффективности лечения язвенного колита, выполненного в форме ректальных суппозиторий изготовленного из масла гранатовых косточек.

Ключевые слова: язвенный колит, лечение, масло гранатовых косточек, ректальные свечи.

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YARALI KOLITDA ANOR DANAGI MOYI**ANNOTASIYA**

Anor danagi moyi murakkab yog' kislotalari to'plamidan iborat bo'lib, ularning taxminan 80% uchta o'zgaruvchan qo'sh bog'lanishga ega 18 uglerodli molekulalardir. Hayvonlarda o'tkazilgan tajribalarda anor danagi moyi antioksidant, o'smaga, yallig'lanishga qarshi faolligi

aniqlangan. Tadqiqotimizning maqsadi anor danagi moyidan tayyorlangan rektal shamchalar yarali kolitni davolash samaradorligini oshirishdir.

Kalit so'zlar: yarali kolit, davolash, anor danagi yog'i, rektal shamchalar.

Introduction. The incidence rates of ulcerative colitis (UC) vary widely in the world and in Uzbekistan, but they allow us to confidently talk about growth. Of particular importance is the increase in the incidence of UC in young able-bodied citizens, as well as the high probability of complications after these diseases.

At least 30% of patients with UC are refractory to therapy, many have a wide range of side effects that limit the use of drugs. In this regard, alternative therapeutic strategies for UC are the focus of attention of many research groups, may include the use of prebiotics, mesenchymal stem cells, tolerant cytokines and cells, etc. The development of new, pathogenetically proven and safe medicines, mainly of local action with active substances of endogenous or plant origin, is in demand. In experimental and clinical conditions, the effectiveness of the use of herbal remedies such as *Boswellia serrata*, *aloe vera*, *andrographis paniculata*, *ellow elm*, and many others has been demonstrated, which is largely due to the presence of polyphenols and flavonoids in their composition. In this regard, pomegranate seed oil attracts attention, the pleiotropic effects of which, including antioxidant, cytoprotective, anti-apoptogenic, anti-inflammatory, immunomodulatory, antimicrobial, etc., have been demonstrated in clinical and experimental conditions in rheumatoid arthritis, uveitis, atherosclerosis, and other diseases, suggesting its effectiveness in ulcerative colitis. There are no registered dosage forms containing pomegranate seed oil in Uzbekistan, with the exception of biologically active additives, which significantly limits its study and possibilities for use in ulcerative colitis.

Candles for rectal use are known to contain diosmin, dexpanthenol, green tea extract, and excipients in the form of an emulsifier and fatty acid glycerides, with the following component ratios:

Diosmin 0.3 - 0.65 g, dexpanthenol - 0.05 - 0.2 g, green tea extract - 0.05 - 0.2 g, emulsifiers and glycerides of fatty acids - 0.0135 - 0.1825 g (RF patent No. 2545994).

The disadvantage of such candles is that a large number of additional substances that are not directly medicinal products carry the risk of allergic reactions. The technological process of manufacturing such a multicomponent drug is very complex.

There is also a herbal medicine made in the form of a suppository containing a dry extract of the rhizome of *turmeric longa* (*Curcuma longa* L.), standardized for curcumin, benzocaine and pharmaceutically acceptable fillers.

The product contains a dry extract of turmeric rhizome long, standardized for curcumin, benzocaine and a suppository base at their ratio per 1 suppository weighing 1 g: dry extract of turmeric rhizome 25-100 mg long, benzocaine (anesthetic) 25 mg, suppository base (vitepsol or cocoa butter) the rest (RF patent No. 2288735).

However, the effectiveness of the drug is not high enough, due to the fact that curcumin is poorly absorbed into the blood, and therefore the effectiveness of the drug decreases.

The purpose of the study: to develop a remedy for the topical treatment of ulcerative colitis.

Material and methods. We have produced a real remedy for the local treatment of ulcerative colitis, made in the form of a suppository, including cocoa butter and vitepsol as a suppository base, the active ingredient contains pomegranate seed oil as an active ingredient, with the following ratio per 1 suppository weighing 3 g: pomegranate seed oil 0.5g, cocoa butter 0.1g, vitepsol 2.4 g.

A patent was obtained for a utility model of the Republic of Uzbekistan No. FAP 2572 "A remedy for the treatment of inflammatory diseases of the rectum" (08/21/2024).

The proposed remedy is obtained as follows.

Before starting the technological process, all laboratory equipment, dishes (mortars) and molds are sterilized, cleaned and cooked at room temperature of 25 ° C.

Suppository bases heated to 38 ° C are dissolved in the amount indicated in the above table. 0.1 g of cocoa butter and 2.4 g of vitepsol are slowly mixed with a homogenizer mixer. 0.5 g of pomegranate oil is added to it and mixed well. The mass should be warmed up carefully, the temperature should not exceed 42 ° C. When it overheats, the quality of the cooked candles deteriorates.

The composite masses are mixed until a homogeneous base is formed, and after preheating the masses to 38 ° C and thinly lubricating the inner walls of the molds with petroleum jelly, they are poured into molds and placed in the refrigerator for 15 minutes.

The obtained suppositories with pomegranate seed oil are white suppositories of the same size, the surface is smooth and torpedo-shaped, without mechanical additions.

The drug is used for the prevention and treatment of hemorrhoids, proctosigmoiditis, paraproctitis, cracks, fistulas and tumors of the rectum.

Pomegranate seed oil mainly consists of triglycerides containing unsaturated fatty acids, including high levels of conjugated linolenic acids (CLA; 78-86%), followed by oleic acid (4-7%, 18:1n-9), linoleic acid (LC; 3-6%, 18:2n-6), palmitic acid (2-3%, 16:0) and stearic acid (2%, 18:0) (Sassano G, Sanderson P, Franx J, Groot P, van Straalen J, Bassaganya-Riera J. Analysis of pomegranate seed oil for the presence of jacaric acid. J Sci Food Agric 89: 1046–1052, 2009). Pomegranate seed oil CLA consists of seven geometric isomers of 9,11,13-octadecatrienoic acid (18:3) separated by a single carbon-carbon bond, unlike the methylene groups in linolenic acid (18:3h-3). The main CLA in pomegranate seed oil is pomegranate acid (HA; 57-71%) [5]. Structurally, pomegranate acid is a C18 carbon fatty acid containing cis-9, trans-11, and cis-13 double bonds (cis-9, trans-11, and cis-13-octadecatrienoic acid) [7].

Pomegranate seed oil, which is the main source of conjugated linolenic acids such as pomegranate acid, has strong anti-inflammatory properties. A study by Christine F. Coursodon-Boyiddle et al. [8] evaluated the effect of orally administered pomegranate seed oil on the development of necrotizing enterocolitis (NEC), intestinal epithelial proliferation, and cytokine regulation in a rat model of NEC. Intestinal damage, epithelial cell proliferation, cytokine production, and trefoil factor 3 (Tff3) were evaluated in the terminal ileum. Oral administration of pomegranate seed oil reduced the incidence of NEC from 61% to 26%. The feed mixture with pomegranate seed oil improved the proliferation of enterocytes at the site of injury. Elevated levels of pro-inflammatory IL-6, IL-8, IL-12, IL-23, and TNF- in the ileum of rats treated with pomegranate seed oil returned to normal. In conclusion, the introduction of pomegranate seed oil protects against NEC in a model of newborn rats. This protective effect is associated with improved intestinal epithelial homeostasis and a pronounced anti-inflammatory effect of pomegranate seed oil on the developing intestinal mucosa.

Pomegranate seeds are a source of many useful substances. They are rich in vitamins (A, E, groups B, C, PP), minerals (phosphorus, iron, calcium, sodium, iodine, potassium, etc.), tannins, fatty oils, antioxidants, phytohormones.

Experimental studies have shown that pomegranate seed oil is able to reduce the occurrence of tumors both in ex vivo and in vivo rodent models [8]. In addition, recent studies show that pomegranate acid facilitates the course of colitis.

Results. The resulting suppositories are amber in color, torpedo-shaped.

Store in a dry place protected from light at a temperature not exceeding 25 ° C. Shelf life: 2 ears. After the expiration date, do not use the drug.

Contraindications:

- pregnancy;
- breastfeeding;
- children under 1 ear of age;

hypersensitivity to the components of the drug.

Clinical trials were conducted on volunteers.

Suppositories were prescribed to adults and children with inflammatory diseases of the rectum (hemorrhoids of moderate and mild severity, proctitis, proctosigmoiditis and paraproctitis, as well as cracks, fistulas of the rectum).

The method of administration and dosage.

Before the suppository is administered, the intestines must be emptied. The suppository should be inserted into the anus with a pointed end, as deep as possible. For more convenient insertion of the suppository, it is recommended to bend down, squat or lie on your side with your legs tucked under.

Dosage regimen:

Adults are prescribed 1 suppository (250 mg) 2 times a day, morning and night; the maximum single dose is 250 mg; the maximum daily dose is 500 mg.

Children aged 1-7 years are prescribed 1 suppository (125 mg) 2 times a day, morning and night; the maximum single dose is 125 mg; the maximum daily dose is 250 mg.

Children aged 7-12 years are prescribed 1 suppository (125 mg) 2 times a day, morning and night; the maximum single dose is 125 mg; the maximum daily dose is 250 mg.

Children over 12 years of age are prescribed 1 suppository (250 mg) 2 times a day, in the morning and at night; the maximum single dose is 250 mg; the maximum daily dose is 500 mg.

The duration of treatment with the drug for inflammatory diseases ranges from 7 to 30 days, depending on the severity of the disease. In case of oncological diseases, there are no restrictions on the duration of use of the drug.

Side effect: When used according to the indications in the recommended doses, no side effects were detected.

Interaction with other drugs: when used simultaneously, candles weaken the effect of aminazine and barbiturates.

With hypersensitivity to the drug, irritation of the mucous membrane of the rectum may occur, in some cases pain in the rectum.

The combined drug for topical use has pronounced anti-inflammatory, antimicrobial, immunomodulatory, reparative, antioxidant, analgesic and anticancer effects.

The use of candles made from pomegranate seed oil allows you to achieve high results in the treatment of such intractable diseases as cracks, ulcers and anal fistulas. These diseases are difficult to treat therapeutically, since the pain symptom characteristic of these diseases causes spasm of the muscles of the rectum, disrupting the blood circulation of this organ and, thereby, preventing the healing of its damage.

Direct organotropic toxic effects and allergic reactions are extremely rare [8].

Conclusion. The safety of pomegranate seed oil, as well as their healing properties, largely determined by the common origin and structure of plant, higher animal and human cells, makes it possible for them to be successfully used in geriatrics. This "kinship" determines the proximity of their chemical composition, the similarity of the course of the most important biochemical processes, and, as a result, a mild, adapted reaction of the organism of higher animals and humans to the administration of this drug of biological origin. When using granola seed oil, direct organotropic toxic effects, allergic reactions, and addiction syndrome are extremely rare. Therefore, they can be used with reliable safety for long-term courses, as well as prescribed to categories of patients with an increased risk of side effects from synthetic drugs, including elderly and senile patients, especially in the presence of renal or hepatic insufficiency. Against this background, if necessary, other drugs from various pharmacotherapeutic groups can be prescribed without the risk of undesirable interactions. Before discussing drugs that have a normalizing effect on the processes of free radical oxidation of lipids, it is necessary to pay attention to the importance of lipids in the energy supply of the myocardium [7]. It is this link of pathogenetic mechanisms that is the point of application of various antioxidants. Antioxidants are compounds of various chemical natures that can break the chain of free radical peroxidation reactions or directly destroy peroxide molecules. Antioxidants are involved in sealing the membrane structure, which reduces the availability of oxygen to lipids.

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