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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

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GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებშიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman (Кириллица)**, для текста на грузинском языке следует использовать **AcadNusx**. Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - <http://www.spinesurgery.ru/files/publish.pdf> и http://www.nlm.nih.gov/bsd/uniform_requirements.html В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректур авторам не высылаются, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface - **Times New Roman (Cyrillic)**, print size - 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf

In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned
Requirements are not Assigned to be Reviewed.**

ავტორთა საქურაღებოლ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დაიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx**. შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფხიხლებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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INFLUENCE OF PAPAVERINE AND COMMERCIAL DIETARY SUPPLEMENTS ON BLOOD GLUCOSE AND BODY WEIGHT IN OBESE DOGS

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Abstract.

Our experiments showed that papaverine inhibits sugar absorption in vivo as well as in vitro. Papaverine blocks the absorption of sugar both in healthy and diabetic animals. Oral administration of papaverine significantly reduced blood sugar level but after an hour blood sugar level showed tendency to come back to the initial levels that were characteristic for these diabetic dogs. Dietary supplement made of herbal remedies and papaverine has proven to be quite effective in reducing body weight in dogs. For a month, dogs with initial overweight lost on average more than 1 kg (10+ %), that is a very good result for their size.

Key words. Papaverine, sugar, absorption, small intestine, blood glucose level, dietary supplements, overweight.

Introduction.

Papaverine (from lat. papaver "poppy") is an opium alkaloid, an isoquinoline derivative, a drug of antispasmodic and hypotensive action. Isolated from opium and studied in 1848 by Georg Merck (1825-1873). G. Merck was the son of Emmanuel Merck (Merck, 1794-1855), the founder of Merck Corp., the largest German chemical and pharmaceutical company. Georg Merck was a student of the famous German chemists Justus Liebig and August Hofmann [1].

According to its purpose, papaverine refers to antispasmodics of widespread use. Once in the body, the drug is able not only to relieve spasm of smooth muscles, but also to relax the vessels, allowing them to expand, and also to relieve spasm from the respiratory system, for example, from the bronchi. As a result, it improves blood circulation and tissues receive more oxygen [2]. Special doses of the drug can reduce cardiac excitability and affect the central nervous system. It is an inhibitor of the enzyme phosphodiesterase and causes intracellular accumulation of cyclic 3, 5-adenosine monophosphate, which leads to impaired contractility of smooth muscles and their relaxation in spastic conditions. Papaverine does not have narcotic properties but has long been used as a smooth muscle relaxant to treat vasospasm and erectile dysfunction. Its vascular effects were thought to be related to its activity as a phosphodiesterase 10A inhibitor. Fibrosis at the injection site - a side effect associated with long-term use of the drug [3,4,5].

During the study, it was found that papaverine reduces tumor hypoxia and enhances the response to radiation therapy. Papaverine or one of its derivatives appears to be ideal candidates for radio sensitization. Scientists believe that the added benefit

of papaverine in combination with stereotactic radiotherapy (SLT) will be beneficial in malignancy [4,5].

Glucose, along with fatty acids and ketone bodies, is an essential source of energy. The level of glucose in the blood is maintained at a constant 4-6 mM (0.8-1.0 g/l) due to the fine regulation of the processes of its intake and consumption. Glucose comes from the intestines (through the food digestion), liver and kidneys. In this case, the liver performs the function of "glucostat": in the phase of resorption, glucose enters the liver from the blood and accumulates in the form of glycogen. In case of glucose deficiency (postresorption phase, starvation), the liver, on the contrary, supplies glucose, which is formed due to the processes of glycogenolysis and gluconeogenesis [6,7].

Diabetes mellitus is one of the most common endocrine disorders in dogs. Mostly middle-aged and elderly dogs (7-10 years old) are ill. There is a gender bias. Diabetes mellitus is predominantly recorded in unsterilized females. In this case, it occurs under the influence of contrainsular hormones: progesterone and somatotrophic hormone. After the end of oestrus, the concentration of progesterone in the blood of dogs increases. High concentrations of progesterone in the blood stimulate the process of secretion of somatotrophic hormone by mammary gland tissue, which is typical for dogs. Both progesterone and growth hormone, being contrainsular hormones, increase tissue resistance to the action of insulin. That is, there will be a relative insufficiency of insulin. Under the current conditions, beta cells responsible for the synthesis and secretion of insulin are forced to be in a state of hyperfunction to ensure normal glucose concentration by increasing the concentration of insulin in the blood. In the past it was shown that papaverine inhibits glucose transport in extirpated rats' small intestine in vitro [8,9]. This effect was never verified in vivo. We conducted such a study on dogs by measuring blood sugar level. The main goal of the present research was to find an additional way to control blood sugar level and body mass in diabetic and overweight animals.

Materials and methods.

Mix-breed, medium size (average 12-15 kg), 2-5 years old, castrated dogs were tested in the morning after a night without access to food. All experiments were performed under licensed veterinarian supervision and permission of their owner. Experiments did not need any painful procedure.

One group of animals included five healthy dogs. The second group included four dogs that were previously diagnosed as diabetic. At the morning experiment, diabetic dogs did not get their regular insulin injection.

The scheme of the experiment was the same in both groups. Blood glucose level was measured by glucose meter “Advocate”. Units of blood sugar measurements are mg/dl.

Blood sugar measuring was executed before breakfast (150 g of dry EN “Purina” food). Then blood testing was performed 30 minutes after breakfast followed by oral administration of papaverine (“MR Papaverini hydrochloridum” 2% sterile solution). Three doses were tested - 0.5 ml, 1.5 ml, or 3 ml, and after that we measured blood sugar level every 30 minutes. Body mass control was performed by weighing animals at the same day time.

Testing of commercial herbal supplements were performed under conditions maximally imitated regular practice and convenience of pet owners. The experimental animals were kept in normal household conditions and received a normal diet with normal physical activity. Pet owners receive D-28, D-29, and D-30 nutritional supplements with instructions to give the animals a teaspoon twice daily. The exact composition of D-28, D29 and D30 is VetVittels know-how, but its main ingredients were papaverine and extracts of hibiscus, fenugreek, and ginseng, which were carried in coconut oil, providing a comfortable texture and appealing taste to dogs.

D-29 and D-30 supplements lacked papaverine, and D-30 supplements also lacked ginseng. The observation of the animals lasted a month during which the weight of the animals and the degree of rise in the level of blood glucose after a trial breakfast were monitored weekly.

Statistical verifications were performed according to the standard calculations [10,11].

Results.

As seen on Table 1, the initial blood sugar level was normal (within the standard recommended range) for all healthy animals, and it was between 80 and 90 mg/dl. Soon after breakfast, it raised 25-35 %. Just after oral injection of 0.5 ml of papaverine solution, blood sugar level reduced and reached initial level in an hour. After two hours a slight increase of blood glucose level was registered (Table 1).

Then we verified the effect of higher (1.5 ml versus 0.5 ml) dosages of papaverine under the same conditions as above on the next day on the same group of dogs. The 1.5 ml dose of papaverine solution caused deeper reduction of blood sugar level after the breakfast and this effect lasted somewhat longer but at the end of testing time, it comes to almost initial level (Table 1).

As can be seen from table 1 reliable ($P < 0.05$) differences were registered regarding significant raise of blood sugar level soon after breakfast. 30 minutes after breakfast and administration of papaverine this parameter reliably goes down with the tendency of correlation between the degree of such fall and the dosage of papaverine. Another reliable difference was noted regarding slight raise at the end of the curve (210 min) – less dosage of papaverine correlates with faster raise (see Table 1).

In a separate experiment, we tested the papaverine effect on blood sugar level (Table 2). It appears that without food no significant changes in blood sugar level could be observed both in healthy dogs and dogs with diabetes. (Table 2).

As we can see from this data dogs with diabetes had significantly elevated initial level of blood sugar while fasting (250+ mg/dl for diabetic animals versus 88-90 mg/dl for healthy ones). The increase of blood sugar level after the breakfast was also significantly higher than in healthy animals (350+ mg/dl for diabetic animals versus 140-150 mg/dl in healthy ones). Oral administration of papaverine significantly reduced blood sugar level but after an hour blood sugar level showed tendency to come back to the initial levels that were characteristic for these diabetic dogs (Table 3).

Our experiments now showed that papaverine inhibits sugar absorption in vivo as well as in vitro which was shown before [4,8,9]. It looks like papaverine blocks the absorption of sugar both in healthy and diabetic animals.

On an empty stomach, effect of papaverine in healthy or diabetic animals is undetectable (Tables 1 and 3), which means that inhibition occurs only during absorption of external sugar and elevated level of blood sugar in diabetic animals is

Table 1. Healthy dogs' ($n=5$) glucose blood level after breakfast followed by administration of papaverine (0.5 ml, 1.5 ml and 3.0 ml), mg/dl.

Time, min	Initial before breakfast (0 min)	30 min (after breakfast before papaverine administration)	60 min (30 min after papaverine administration)	90 min (60 min after papaverine administration)	120 min (90 min after papaverine administration)	150 min (120 min after papaverine administration)	180 min (150 min after papaverine administration)	210 min (180 min after papaverine administration)
Control	88 ± 4	149 ± 10	150 ± 5	125 ± 6	116 ± 6	100 ± 6	93 ± 6	90 ± 6
Papaverine dose 0.5 ml	88 ± 3	144 ± 8	120 ± 5*	77 ± 3*	76 ± 4*	75 ± 5*	76 ± 6	95 ± 6
Papaverine dose 1.5 ml	85 ± 5	154 ± 10	102 ± 7*	77 ± 5*	73 ± 4*	80 ± 8	78 ± 5	77 ± 6
Papaverine dose 3.0 ml	86 ± 5	154 ± 9	100 ± 6*	76 ± 6*	70 ± 4*	74 ± 5*	77 ± 4*	76 ± 5

Notes: * – reliable difference compared to control – healthy dogs' blood glucose level after the breakfast ($P < 0.05$).

Table 2. Blood sugar level of healthy dogs ($n=5$) and dogs with diabetes ($n=4$) without food, mg/dl.

Time, min	0	30	60	90	120	150	180	210
Healthy dogs	88 ± 5	90 ± 4	89 ± 6	87 ± 6	85 ± 6	88 ± 7	85 ± 5	87 ± 8
Dogs with diabetes	254±15*	270±12*	240±13*	248±10*	255±12*	290±20*	260±17*	243±15*

Notes: * – reliable difference compared to healthy dogs' blood glucose level ($P < 0.05$).

Table 3. Diabetic dogs' (n=4) blood level curve after breakfast followed by administration of papaverine (0.5 ml, 1.5 ml and 3.0 ml), mg/dl.

Time, min	Initial before breakfast (0 min)	30 min (after breakfast before papaverine administration)	60 min (30 min after papaverine administration)	90 min (60 min after papaverine administration)	120 min (90 min after papaverine administration)	150 min (120 min after papaverine administration)	180 min (150 min after papaverine administration)	210 min (180 min after papaverine administration)
Control	255±15	361±17	345±15	327±12	286±10	290±18	246±16	244±18
Papaverine dose 0.5)	254±15	365±18	325±15	287±9**	256±10	260±14	226±16	249±18
Papaverine dose 1.5 ml	256±16	359±18	288±10**	277±8**	260±9	280±8	240±15	250±11
Papaverine dose 3.0 ml	249±17	364±19	290±11**	260±9**	244±8**	240±5**	250±10	256±11

Notes: ** – reliable difference compared to control – diabetic dogs' blood glucose level after the breakfast ($P < 0.05$)

Table 4. Effect of D-28 Dietary Supplement on Body Weight in Overweight Dogs (n=4).

One week from start of observation	0	1	2	3	4
Weight, kg	11.5 ± 0.5	11.3 ± 0.6	10.9 ± 0.5	10.5 ± 0.5	10.2 ± 0.4
Weight, % of the initial	100	98.1	94.5	91.2	88.7

Table 5. Effect of D-29 Dietary Supplement on Body Weight in Overweight Dogs (n=5).

One week from start of observation	0	1	2	3	4
Weight, kg	13.2 ± 0.5	13.3 ± 0.6	12.9 ± 0.5	13.0 ± 0.5	12.8 ± 0.4
Weight, % of the initial	100	101	98	98	97

Table 6. Effect of D-30 Dietary Supplementation on Body Weight in Overweight Dogs (n=4).

One week from start of observation	0	1	2	3	4
Weight, kg	10.5 ± 0.5	10.3 ± 0.6	10.2 ± 0.5	9.6 ± 0.5	9.9 ± 0.4
Weight, % of the initial	100	98	97	91	94

supported by glucose coming from internal storages. Note: there is no tradition in veterinary medicine to distinguish diabetes 1 and 2 types in dogs [5].

On our recommendation, VetVittels LLC has made several supplements for overweight dog that we have tested. In total, three recipes were tested, differing in the proportion of medicinal herbs included in them. The exact recipe for the composition of nutritional supplements is the know-how of VetVittels LLC and can only be published after obtaining a patent.

Supplement D-28 appeared the most potent supplement compare to D29 and D30. Its main difference is the presence of papaverine.

From the data in Table 4, it can be seen that the D-28 dietary supplement for weight loss in dogs was quite effective. Over the course of a month, dogs with initial overweight lost an average of more than 1+ kg (>10 %), which is a very good result for their size. The food supplement D-29 turned out to be practically ineffective (Table 5) - after a month of its use, the weight of the animals decreased by only 3%, which is unreliable.

Dietary supplement D-30 had some positive effect on weight loss in dogs but was inferior in effectiveness to dietary supplement D-28 - the reduction in body weight in this case was 6% compared to 11% when using dietary supplement D-28 (Table 6).

Discussion.

Our experiments now showed that papaverine inhibits sugar absorption in vivo as well as in vitro which was shown before. The inhibitory effect of papaverine on glucose absorption was demonstrated in experiments on three species – rats, guinea pigs and dogs and it can be observed in different types of cells (enterocytes and cardiocytes). It blocks the absorption of sugar both in healthy and diabetic animals [3,5,9,12].

It also should be noted that there is a definite limit for papaverine needed for complete inhibition of sugar absorption. Oral administration of 0.5 ml of papaverine solution caused significant reduction in glucose absorption and this effect became even more significant when the amount of inhibitor was tripled to 1.5 ml, but an additional increase in dose to 3 ml had no effect.

The correlation between elevated blood sugar level and tendency to gain extra weight is doubtless now [13]. Methods which inhibit sugar absorption in the intestine may cause the loss of high-caloric substances for eater's body. They probably will be utilized by microflora of the gut which means that that host organism being well-fed do not get extra calories for gaining weight. Based on this logic we consider that papaverine added to supplements can be an effective method of weight control.

Conclusion.

Therefore, it looks like papaverine after an additional research can be added to the list of pharmaceuticals that prevents sugar absorption in intestine for blood sugar control and/or weight loss.

Dietary herbal supplement with papaverine (D-28) has proven to be quite effective in reducing body weight in dogs. For a month, dogs with initial overweight lost on average more than 1 kg (10+%), that is a very good result for their size.

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