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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.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

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 ВИНИТИ 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 ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

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. Корректура авторам не высылается, 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 compu-ter-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 საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ 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 შეღებვის 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 ფჩხილებში 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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BLOOD AND CYTOGENETIC MARKERS IN EXPERIMENTAL BURNS AND THEIR TREATMENT WITH $[CU(L^{CF3})_2]$ AND $[CU(ADM)(PPH_3)_2]PF_6$

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Abstract.

The search for effective agents in the treatment of burn injuries is one of the urgent problems of combustiology. Over the past years, the incidence of burn injury has been continuously increasing worldwide. In burn injury, there is not only local tissue damage in the area of action of the offending agent, but also a complex reaction of the body to the resulting damage in the form of burn disease. Summing up the karyotyping results under thermal burn, it can be concluded that the intraperitoneal administration of compounds $Cu(L^{CF3})_2$ and $[Cu(Adm)(PPh_3)_2]PF_6$ has a corrective effect on hemorheological and hemodynamic disorders occurring in thermal burn. This effect is most pronounced in the first days after correction. According to the results of karyotyping under thermal burn, it can be stated that the compound $[Cu(Adm)(PPh_3)_2]PF_6$ has the most positive results, and the compound $Cu(L^{CF3})_2$ was less effective. This fact is confirmed when comparing survival, cytogenetic parameters, and blood parameters after administration of these compounds. Cytogenetic abnormalities were recorded during the burn injury. When correcting $[Cu(Adm)(PPh_3)_2]PF_6$, a tendency towards increased proliferation is observed both on the 15th and 30th days. The chromosomal aberrations and the number of polyploid cells were statistically significantly reduced in the group with $[Cu(Adm)(PPh_3)_2]PF_6$ application relative to the pure thermal burn group in both the 15th and 30th days, indicating the beneficial effect of this copper complex on the burn.

Key words. Experimental burn, mitotic index, chromosomal aberrations, polyploid cells.

Introduction.

Burn injuries are a major global medical challenge, with their incidence steadily increasing in recent years. Burn injury is characterized not only by localized tissue damage in the area of action of the damaging agent, but also by a complex systemic response known as burn disease. According to the World Health Organization (WHO), burns are the third most common type of injury. In wartime, they have accounted for 0.4-0.8% of all fatalities [1].

The severity of tissue damage depends on the degree of overheating, with higher temperatures leading to more rapid cell death. The depth of a burn injury depends on the thermal agent's characteristics, temperature, duration of exposure and the extent of heat penetration into deeper layers of the skin and underlying tissues. Key pathophysiological factors in thermal injuries include a pronounced sympathoadrenal response with activation of stress-related structures, and mechanisms, accompanied by disturbances in the microcirculation system. Additionally, erythremia occurs as a result of increased loss of the liquid part of the blood from the vessels due to their increased permeability and through damaged skin [2]. Burn injuries not only affect the damaged site but also cause systemic changes in unaffected organs and tissues. The movement of fluid from the intravascular bed to the extravascular space and exudation lead to thickening of the blood or anemia. The cause of anemia is the red blood cells destruction due to the direct influence of elevated temperature and as a result of stasis and reduced osmotic resistance [3-6].

Circulatory and microcirculatory disorders, leading to deterioration of perfusion in organs and tissues, are key pathological processes in the development of a systemic inflammatory response. From this point of view, intensive therapy aimed at maintaining effective hemodynamics during the burn shock phase is crucial for preventing the development and minimizing the manifestations of multiple organ dysfunction syndrome [7-9].

The severity of a thermal injury is determined by several factors, with the most critical being the extent and depth of the burns (determining the surface area and degree of burns). Medical treatment for burns is crucial, especially when they are III degree burns and when a significant surface area of the body is affected [10-12].

One of the priority tasks in medicine is the search for new, effective compounds that can be used to minimize and protect against thermal injuries. In this regard, coordination complexes with high antioxidant activity are of particular interest. Studies have highlighted their ability to protect the body from the damaging effects of thermal burns, as reported both in the scientific works of some authors [13] and in several studies conducted at the Orbeli Institute of Physiology NAS RA [14-17].

To identify the possible reparative effect of the synthesized chemical copper complexes $[Cu(L^{CF3})_2]$ and $[Cu(Adm)(PPh_3)_2]PF_6$, the study included cytogenetic screening and analysis of blood parameters against the background of a thermal burn.

Materials and Methods.

Synthesis of $Cu(L^{CF3})_2$: The copper(II) complex $[Cu(L^{CF3})_2]$ (Figure 1a) was synthesized by a one-step synthetic protocol involving the reaction of the β-diketone ligand 1,1,1,5,5,5-hexafluoro-2,4-pentanedione (HLCF3) with copper(II) acetate monohydrate, according to general procedures detailed in previous literature [18] for analogous homoleptic copper(II) complexes [19,20].

Synthesis of $[Cu(Adm)(PPh_3)_2]PF_6$:

The copper(I) complex $[Cu(Adm)(PPh_3)_2]PF_6$ (Figure 1b) has been synthesized and fully characterized using both analytical and spectroscopic methods. Tetrakis (acetonitrile) copper(I) hexafluorophosphate (0.500 mmol, 0.186 g) and triphenylphosphine (1.000 mmol, 0.262 g) were dissolved in CH3CN (20 mL), and the reaction was stirred for 2 hours at room temperature. Then, the Amantadine (0.500 mmol, 0.076 g) was solubilized in CH3OH (20 mL) and added to the reaction mixture that was stirred for 24 hours at room temperature. A white suspension was filtered off, the obtained mother liquors were washed with diethyl ether/n-hexane and dried under reduced pressure to give the complex $[Cu(Adm)(PPh_3)_2]PF_6$ in 80% yield. Mp: 203-205°C. Solubility: CH3OH, CH2Cl2, CHCl3, EtOAc, CH3CN, DMSO. FT-IR (cm-1): 3308 (N-H); 3075w, 3058w, 2914wbr, 2850w (C-H); 1586w, 1480m, 1435s, 1371w, 1310w, 1181w, 1163w, 1117w, 1093m, 1026w, 999w, 876w, 859sh, 833vs, 753s, 741s, 693vs, 577s, 541m, 519s. 1H-NMR (Acetone-d6, 293 K): 1.42-3.00 (m, 17H, CHAdm and NH2), 7.27-7.51 (m, 30H, CHAr). 31P{1H}-NMR (CD3CN, 243 K): δ -144.76 (sept, JP-F = 706 Hz), -1.64 (sbr). ESI-MS(+) (major positive ions, CH3CN), m/z (%), 152 (90) [Adm + H]+,

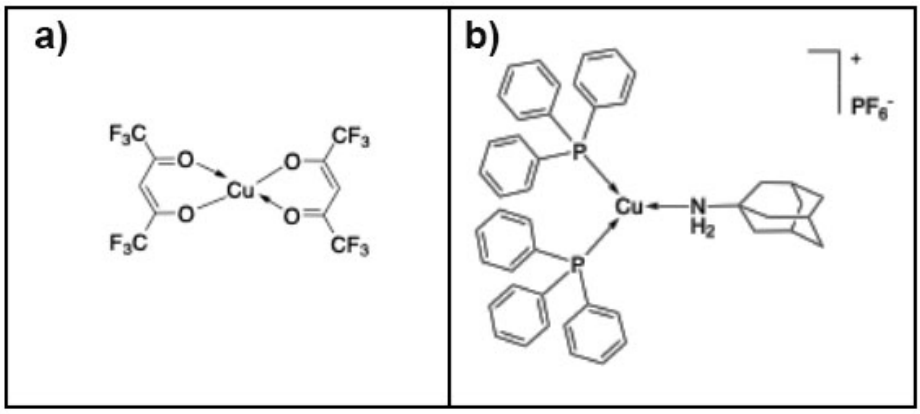

Figure 1. *Chemical structure of $[Cu(L^{CF3})_2]$ (a) and $[Cu(Adm)(PPh_3)_2]PF_6$ (b).*

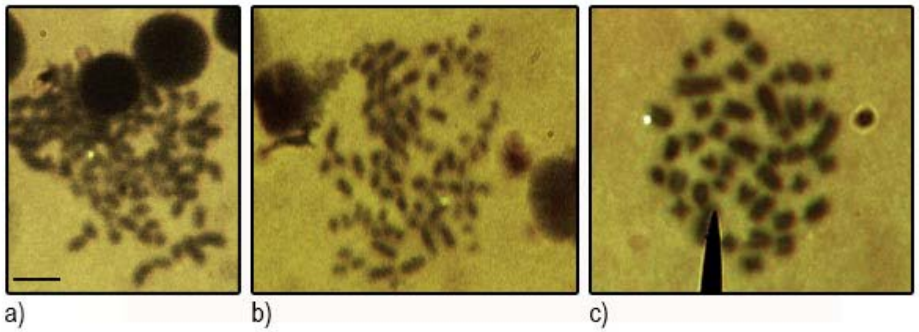

Figure 2. *Bone marrow cells. Polyploid cells (a and b), chromosomal aberrations in the form of a double fragment (c). Magnification: ×900.*

366 (60) [Cu(PPh3) + CH3CN]+, 589 (100) [Cu(PPh3)2]+. ESI-MS(-) (major negative ions, CH3CN), m/z (%): 145 (100) [PF6]-. Elemental Analysis (%) calculated for C46H47CuF6NP3 (%): C 62.48, H 5.36, N 1.58; found: 63.23, H 5.10, N 1.96.

The study investigated changes in hemodynamic parameters following a thermal burn and their correction using the copper complexes $[Cu(L^{CF3})_2]$ and $[Cu(Adm)(PPh_3)_2]PF_6$.

The study was carried out on 40 male albino rats weighing 170-180g. The animals were divided into 4 groups (with 10 animals in each group).

Group I: intact animals (control group).

Group II: pure burn.

Group III: burn + $[Cu(L^{CF3})_2]$.

Group IV: burn + $[Cu(Adm)(PPh_3)_2]PF_6$).

A thermal III-AB degree burn covering 30% of the body surface was applied to the epilated skin on the back of the animals with a hot object (a special plate). The copper compounds $[Cu(L^{CF3})_2]$ (dose 50 mg/kg) and $[Cu(Adm)(PPh_3)_2]PF_6$ (dose 50 mg/kg) were administered intraperitoneally 1 hour after the burn, followed by treatments every other day for the next 10 days. Changes in blood parameters were studied on the 3rd, 7th, 14th, 21st and 30th days after thermal burn.

Survival and cytogenetic parameters were studied using the Ford-Wollam method [21]. The cytogenetic analysis included chromosome examination using Giemsa staining. The mitotic index (MI, in %), chromosomal aberrations (CA, in %) and percentage of polyploid cells (PPC) in animal femur bone marrow cells (counting in 1000 cells per preparation) were determined, according to G. McGregor [22]. Metaphase searches were conducted under a microscope with magnifications of 900 times. Cytogenetic indices were analyzed on the 15th and 30th days. The physicochemical properties of the synthesized compounds were also examined. Data analysis was carried out using the specialized statistical software packages Statsoft and SPSS-10.0. Method of regression and correlation analysis method were used [23].

Results and Discussion.

During the study, the survival rate of animals across the 4 experimental groups was evaluated. In the control group (intact animals), survival was 100%. In Group II (pure burn) it dropped to 60%. In Group III which was injected with $[Cu(L^{CF3})_2]$ after burn, a survival was 80%, and Group IV which was injected with $[Cu(Adm)(PPh_3)_2]PF_6$ after burn, a survival rate of 100%.

Regression analysis yielded logarithmic equations and survival curves as follows:

y1=100+0*lg(x) (intact animals).

y2= 90.39-23.8*lg(x) (pure burn).

y3= 103.82-18.33 *lg(x) (burn + $[Cu (L^{CF3})_2]$).

y4=100+0*lg(x) (burn + $[Cu(Adm)(PPh_3)_2]PF_6$).

These survival equations were used to model the survival of intact animals, animals after a pure burn, animals with burn + $[Cu (L^{CF3})_2]$ and animals with burn + $[Cu(Adm)(PPh_3)_2]PF_6$. According to the obtained equations (where x is the number of days since the day of the start of the experiments, and y is the survival rate), the best result was observed in the group "burn + $[Cu(Adm)(PPh_3)_2]PF_6$" (100%) (compared to the 60% survival rate in the "pure burn" group). The curves also allowed for extrapolation to estimate survival rates over longer periods. The selected concentration of the test compounds during burn proved to be the most effective, as evidenced by the survival rate.

It is known that burn disease causes a pronounced leukocyte reaction [24], therefore, an analysis of blood parameters was carried out to assess the condition of the body of animals that have suffered a burn injury and the healing process. To detect any changes between experimental groups of animals, the following blood parameters were examined: blood clotting time, leukocyte count, thrombocytes count, erythrocyte count, hemoglobin level, and hematocrit.

The analysis of the data allows us to conclude that changes in hemodynamics following a burn (3 days after a thermal burn) are marked by non-specific reactions: a reliable drop in the blood viscosity (compared to intact animals), a sharp increase in blood viscosity, apparently indicating increased erythrocytes aggregation, an increase in the level of hemoglobin and hematocrit, indicating hemoconcentration. The blood parameters of the studied animals are presented in Table 1.

When comparing the hematological indices of experimental rats that received $[Cu(L^{CF3})_2]$and $[Cu(Adm)(PPh_3)_2]PF_6$ intraperitoneally with a "pure burn" group at different time points (3, 7, 14, 21 and 30 days), the following data were obtained: Blood clotting time, significantly decreases starting from the 7th day in both groups. Notably, in both groups receiving the compounds, this indicator retains a reliable change until the end of the observation. In terms of leukocyte levels, there was significant variability across all groups compared to the "pure burn". Specifically, with the administration of $[Cu(Adm)(PPh_3)_2]PF_6$, a more moderate increase in this indicator was observed, indicating a less pronounced inflammatory response. The number of platelets significantly decreases from the 3rd day in both groups compared to the "pure burn" throughout the experiment. The obtained data suggest that the tested compounds somewhat inhibit the platelet germ of hematopoiesis.

In the group treated with $[Cu(Adm)(PPh_3)_2]PF_6$, the tendency to recovery is more pronounced

Regarding the change in erythrocyte count, a reliable increase in this indicator is observed in the 2 injected groups starting from the 7th day, with normalization occurring by the 14th day. Another key red blood cell parameter, hemoglobin, does not show any significant changes compared to the control group in each group throughout the observation period. Hematocrit levels, remain reduced throughout the experiment in response to the injection of the compounds. The data indicate that plasma loss in the control group is higher than in the groups with the injection of the copper complexes. The studied compounds contribute to a decrease in both platelets count and hematocrit percentage, indicating a correlation between these indicators in regulating blood thickening in burns due to plasma loss through the wound surface.

The study of the reparative effect of $[Cu(L^{CF3})_2]$ and $[Cu(Adm)(PPh_3)_2]PF_6$ complexes on the chromosomal apparatus of bone marrow cells on the 15th and 30th days after the burn revealed notable findings. Comparing the karyotype of rats with a "pure burn" that received $[Cu(Adm)(PPh_3)_2]PF_6$, a tendency toward increased proliferation (MI) is noted on both the 15th and 30th days. In the "burn + $[Cu(L^{CF3})_2]$" and "burn + $[Cu(Adm)(PPh_3)_2]PF_6$" groups, the percentage of chromosomal aberrations (CA) significantly decreases compared to the "pure burn"

Table 1. *Hematological parameters in animals on the 3rd, 7th, 14th, 21st, 30th day after the burn. *- p<0.05 reliability criteria for burned animals.*

Indicators	**Compounds**	**Days**				
		3	**7**	**14**	**21**	**30**
Blood clotting	**pure burn**	264.0	215.0	225.6±13.09	277.8±15.77	330.0±18.44
time		±12.88	±14.32			
(seconds)	**+ [Cu(L^{CF3})2]**	308.125±19.97 (*)	157.85±7.93 (*)	136.0±17.71 (*)	259.16±34.07	226.66±28.94 (*)
Norm	**+ Cu(Adm)(PPh3)2]PF6**	231.8±10.94 (*)	207.2±12.16	175.5±10.04 (*)	172.5±6.29 (*)	158.0±14.89 (*)
311.0±19.0						
Leukocytes	**pure burn**	14720.0	16920.0	11320.0	13640	15960.0
(N/μL)		±810.0	±618.0	±890.0	±670.0	±460.0
	+ [Cu(L^{CF3})2]	17050.0	22133.3	18810.0	18283.33	10933.73
Norm		±692.56 (*)	±1062.91 (*)	±1405.03 (*)	±1396.76 (*)	±588.03 (*)
11500.0 ±420.0	**+ Cu(Adm)(PPh3)2]PF6**	17120.0 ±672.77 (*)	20920.0 ±2535.473	14500.0 ±780.456 (*)	15730.0 ±950.561	16130.0 ±735.761
Thrombocytes	**pure burn**	627000.0	681400.0	609000.0	590000	571000
(N/μL)		±10793.52	±62572.38	±52115.26	±37524.98	±22934.69
	+ [Cu(L^{CF3})2]	386875.0	310333.3	348000.0	429166.7	476666.7
Norm		±29624.7 (*)	±25834.95 (*)	±5524.38 (*)	±33226.91 (*)	±24415.39 (*)
522000.0 ±10560.0	**+ Cu(Adm)(PPh3)2]PF6**	363500.0 ±13764.89 (*)	426500.0 ±23840.33 (*)	515500.0 ±20554.13	511000.0 ±25372.78	509000.0 ±18178.13(*)
Erythrocytes	**pure burn**	5920000	3130000	3560000	6470000	6380000
(N/μL)		±130000	±1000000	±180000	±104000	±190000
	+ [Cu(L^{CF3})2]	5997500.0	6331667.0	5754000.0	5278333.0	4364000.0
Norm		±296959.3	±285918.6	±571861.9 (*)	±461688.3 (*)	±973851.12 (*)
5823000.0 ±278800.0	**+[Cu(Adm)(PPh3)2]PF6**	6310000 ±208273.3 (*)	5760500 ±382418.1 (*)	5163000 ±258805.2	5425000 ±199199.8 (*)	5740000± 243675.6(*)
Hemoglobin	**pure burn**	135.7±3.816	135.9±5.4	144.4±6.02	144.6±5,43	143.6±5,28
(g/L)	**+ [Cu(L^{CF3})2]**	143.76±7.35	144.7±3.79	124.54	136.92	137.3
Norm				±7.27 (*)	±4.72	±3.79
138.1±5.82	**+[Cu(Adm)(PPh3)2]PF6**	142.83±3.01	145.0±2.6	146.78±1.98	148.19±2.06	148.85±1.82
Hematocrit	**pure burn**	46.7±1.4	49.1±0.91	47.3±1.11	48.3±1.18	44.5±1.71
(%)	**+ [Cu(L^{CF3})2]**	51.62±4.12	37.84±4.97 (*)	40.32±3.79	40.0±1.88 (*)	42.94±3.13
Norm						
57.2±1.75	**+[Cu(Adm)(PPh3)2]PF6**	46.09±1.87	46.31±1.94	49.9±1.88	48.31±1.84	49.36±1.42 (*)

Table 2. *Summary table of cytogenetic indices in rats subjected to thermal burns of III–AB degree (30% of body surface) with intraperitoneal administration of [Cu(L^{CF3})$_2$] and [Cu(Adm)(PPh_3)$_2$]PF_6. P1,3, P2,3, P1,4, P2,4 - A statistically significant difference when comparing the indicators of Group I (index 1) and Group II (index 2) with Group III (index 3) and Group IV (index 4).*

Groups Indicators	**Intact**	**Pure burn**	**Burn + [Cu(L^{CF3})$_2$] (15 days)**	**Burn + [Cu(L^{CF3})$_2$] (30 day)**	**Burn + [Cu(Adm)(PPh_3)$_2$]PF_6 (15 days)**	**Burn + [Cu(Adm)(PPh_3)$_2$]PF_6 (30 days)**
MI в %	**20.35±2.8**	**14.2±1.9**	**16.2±1.7** $P_{1,3}$>0.05 $P_{2,3}$>0.05	**16.4±1.4** $P_{1,3}$>0.05 $P_{2,3}$>0.05	**17.2±0.2** $P_{1,4}$>0.05 $P_{2,4}$>0.05	**17.8±0.22** $P_{1,4}$>0.05 $P_{2,4}$>0.05
CA в %	**2.6±0,.6**	**4.2±0.3**	**3.4±0.25** 0.02<$P_{1,3}$<0.05 0.02<$P_{2,3}$<0.05	**3.2±0.42** $P_{1,3}$>0.05 0.02<$P_{2,3}$<0.05	**3.2±0.4** $P_{1,4}$>0.05 0.02<$P_{2,4}$<0.05	**2.9±0.35** $P_{1,4}$>0.05 0.01<$P_{2,4}$<0.02
PC в %	**0.5±0.08**	**3.3±0.36**	**2.6±0.14** $P_{1,3}$<0.001 $P_{2,3}$>0.05	**2.1±0.32** $P_{1,3}$<0.001 0.01<$P_{2,3}$<0.02	**2.4±0.3** $P_{1,4}$<0.001 0.02<$P_{2,4}$<0.05	**2.0±0.3** $P_{1,4}$<0.001 0.002<$P_{2,4}$<0.01

group at both study periods (15 and 30 days after the burn), which indicates a beneficial and long-term effect of both compounds on the burn. During the same observation periods (15 and 30 days after the burn), in two groups that were administered copper compounds (Groups III and IV), there was a significant decrease in the number of polyploid cells (PC) both relative to the intact group (Group I) and relative to animals with a "pure burn" (Group II). The results are summarized in Table 2.

Summarizing the karyotyping results for thermal burns, we can say that the most positive results were obtained with the copper (I) complex [Cu(Adm)(PPh_3)$_2$]PF_6, while the copper (II) complex [Cu(L^{CF3})$_2$] proved to be less effective.

Cytogenetic abnormalities associated with burn injuries to animal skin were analysed. Analysis of bone marrow preparations under a light microscope showed that chromosomal aberrations observed after thermal burn were most commonly double fragments (Figure 2).

Conclusion.

In conclusion, intraperitoneal administration of the copper complexes [Cu(L^{CF3})$_2$] and [Cu(Adm)(PPh_3)$_2$]PF_6 has a corrective effect on hemorheological and hemodynamic disorders associated with thermal burns. This effect is most pronounced during the first day following treatment. According to the karyotyping indices for thermal burn samples, [Cu(Adm)(PPh_3)$_2$]PF_6 compound produces the most positive results. This fact is further supported by comparison of survival, cytogenetic indices, and blood indices after administration of the copper compounds. Additionally, a significant reduction in chromosomal aberrations and the number of polyploid cells was observed in the "burn + [Cu(Adm)(PPh_3)$_2$]PF_6" group compared to the "pure burn" group, at both on the 15th and 30th days of the study. Further research is needed to understand the mechanism by which copper complexes exert a reparative effect on skin after a thermal burn, as well as the mechanism underlying the differential effects of the two copper complexes. However, it is already possible to talk about the reparative (therapeutic) effect of both copper complexes against the background of a thermal burn, as well as the fact that they have the potential to prevent or mitigate the effects of deep burns in animals.

Author contributions.

Study Concept and Design: KAG and SC. Acquisition, Analysis, and Interpretation of the Data: KAG, GVS, SC, PM, DGJ, DAM, PZhH, and FSA. SC and PM synthesized the new compounds KAG, SC, PM, and DMH wrote the manuscript. All of the authors have contributed substantially to the manuscript.

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Availability of data and materials.

Raw data can be provided upon request to the corresponding author.

Declarations:

Competing interests. The authors declare no competing interests.
Conflict of interest. The authors declare no conflict of interest.

Ethical approval and consent to participate.

The experimental protocol corresponded to the conditions of the European Communities Council Directive (2010/63/ UE) and was approved by the Ethics Committee of Yerevan State Medical University after Mkhitar Heratsi (IRB Approval N4, November 15, 2018).

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МАРКЕРЫ КРОВИ И ЦИТОГЕНЕТИЧЕСКИЕ ПАРАМЕТРЫ ПРИ ЭКСПЕРИМЕНТАЛЬНЫХ ОЖОГАХ И ИХ ЛЕЧЕНИИ С ИСПОЛЬЗОВАНИЕМ $[Cu(L^{CF3})_2]$ И $[Cu(Adm)(PPh_3)_2]PF_6$

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Резюме

Поиск эффективных средств лечения ожоговых поражений является одной из актуальных проблем комбустиологии. За последние годы во всем мире наблюдается устойчивый рост числа случаев ожогов. При ожоговой травме наблюдается не только локальное повреждение тканей в зоне действия поражающего фактора, но и сложная реакция организма на полученное повреждение в виде ожоговой болезни. Подводя итоги кариотипирования при термическом ожоге, можно сказать, что наиболее положительные результаты дало соединение $[Cu(Adm)(PPh_3)_2]PF_6$, соединение $Cu(L^{CF3})_2$ оказалось менее эффективным. Можно сделать вывод, что внутрибрюшинное введение соединений $Cu(L^{CF3})_2$ и $[Cu(Adm)(PPh_3)_2]PF_6$ оказывает корригирующее действие на гемореологические и гемодинамические нарушения, возникающие при термическом ожоге. Этот эффект наиболее выражен в первые дни после коррекции. По результатам кариотипирования при термическом ожоге можно констатировать, что наиболее положительные результаты имеет соединение $[Cu(Adm)(PPh_3)_2]PF_6$, соединение $Cu(L^{CF3})_2$ оказалось менее эффективным. Этот факт подтверждается при сравнении выживаемости, цитогенетических показателей и показателей крови после введения этих соединений. В процессе ожоговой травмы зарегистрированы цитогенетические нарушения. При коррекции $[Cu(Adm)(PPh_3)_2]PF_6$ отмечается тенденция к усилению пролиферации как на 15-е, так и на 30-е сутки. Хромосомные аберрации и количество полиплоидных клеток были статистически значимо снижены в группе с нанесением $[Cu(Adm)(PPh_3)_2]PF_6$ по сравнению с группой с чистым термическим ожогом как на 15-й, так и на 30-й дни, что говорит о благотворном влиянии данного комплекса меди на ожог.

Ключевые слова: экспериментальный ожог, митотический индекс, хромосомные аберрации, полиплоидные клетки.