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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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MANIFESTATION OF RADIOPROTECTIVE PROPERTIES IN COPPER COMPLEXES $[CU(L^{CF3})_2]$ AND $[CU(ADM)(PPH_3)_2]PF_6$

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Abstract.

One of the first and direct signs of ionizing radiation's effect on a cell is chromosomes destabilization. By studying cytogenetic indices – including mitotic index, chromosomal aberrations, and the number of polyploid cells in the bone marrow cells of the femur, a significant difference was observed between intact and irradiated animals. This suggests that these indices can be considered as markers of irradiation by the technetium isotope. When assessing the survival rate, the highest survival value was recorded in the Group injected with $[Cu(Adm)(PPh_3)_2]PF_6$. In terms of chromosomal aberrations and number of polyploid cells, irradiated animals showed reliable difference compared to the "irradiation + $[Cu(L^{CF3})_2]$" group at both 15 and 30 days post-exposure, demonstrating the radioprotective property of the compound. Regarding the mitotic index, treatment with $[Cu(L^{CF3})_2]$ showed a trend toward normalization after 15 days, with a reliable difference between Groups 2 and 3 by the end of the study (after 30 days), further supporting the compound's beneficial effect. Analysis of survival, changes in cytogenetic parameters, and multivariate regression analysis when using both complexes confirms the highest efficiency of $[Cu(Adm)(PPh_3)_2]PF_6$ compared to $[Cu(L^{CF3})_2]$. Specifically, treatment with $[Cu(Adm)(PPh_3)_2]PF_6$, in contrast to "pure irradiation", resulted in a significant difference across all parameters and led to the normalization of cytogenetic parameters from the early stages of observation. This suggests a pronounced radioprotective effect of the compound and an accelerated normalization of cytogenetic parameters.

Key words. Irradiation, mitotic index, chromosomal aberrations, number of polyploid cells.

Introduction.

It is well established that the main initiating event after irradiation is DNA damage. Based on this, one of the earliest and most direct indicators of ionizing radiation (IR) effects on cells is the chromosomal destabilization [1,2]. For many years, studies have been conducted to identify sensitive biological markers specific for radiation exposure [3,4]. Radiation-induced karyotype damage is an important indicator for assessing the severity of radiation damage. Radiation-induced alterations of cytogenetic parameters can serve as markers of both adverse effects of IR and efficacy of treatments that enhance the body's resistance.

Currently, chromosomal aberrations in peripheral blood lymphocytes are recognized as key biological markers of radiation exposure [5].

One of the priority tasks of modern radiobiology is the search for new radioprotective compounds. In this area, coordination complexes with high antioxidant activity are of particular interest. Their potential to protect the body from the damaging effects of ionizing radiation has been noted in both independent scientific works [6,7] and research conducted by the L.A. Orbeli Institute of Physiology of the National Academy of Sciences of the Republic of Armenia [8,9]. These studies showed that such complexes have low toxicity and pronounced radioprotective properties.

To release possible radiation-protective actions, we studied compounds of copper-organic complexes: $[Cu(L^{CF3})_2]$and $[Cu(Adm)(PPh_3)_2]PF_6$, which were synthesized in Camerino University (Italy) under the supervision of Professor Carlo Santini. In this study, a cytogenetic screening of these newly synthesized compounds was carried out.

Materials and Methods.

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 (HL^{CF3}) with copper(II) acetate monohydrate, according to general procedures detailed in previous literature [10] for analogous homoleptic copper(II) complexes [11-12].The copper(I) complex $[Cu(Adm)(PPh_3)_2]PF_6$ has been synthesized and fully characterized using both analytical and spectroscopic methods as detailed below.

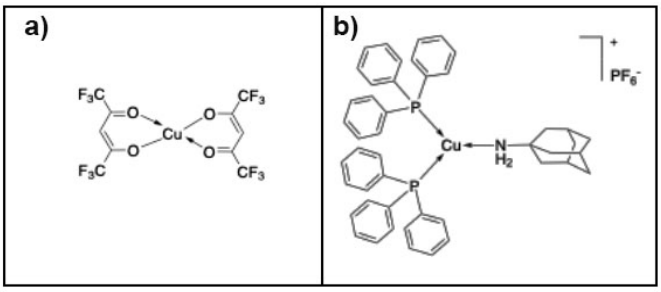

Figure 1. Chemical structure of $[Cu(L^{CF3})_2]$ (a) and $[Cu(Adm)(PPh_3)_2]PF_6$ (b).

Synthesis of $[Cu(Adm)(PPh_3)_2]PF_6$. Tetrakis(acetonitrile) copper(I)hexafluorophosphate (0.500 mmol, 0.186 g) and triphenylphosphine (1.000 mmol, 0.262 g) were dissolved in CH_3CN (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 CH_3OH (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: CH_3OH, CH_2Cl_2, $CHCl_3$, EtOAc, CH_3CN, 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. ^{1}H-NMR (Acetone-d_6, 293 K): 1.42-3.00 (m, 17H, CH_{Adm} and NH_2), 7.27-7.51 (m, 30H, CH_{Ar}). $^{31}P\{^1H\}$-NMR (CD_3CN, 243 K): δ -144.76 (sept, J_{P-F} = 706 Hz), -1.64 (sbr). ESI-MS(+) (major positive ions, CH_3CN), m/z (%), 152 (90) $[Adm + H]^+$, 366 (60) $[Cu(PPh_3) + CH_3CN]^+$, 589 (100) $[Cu(PPh_3)_2]^+$. ESI-MS(-) (major negative ions, CH_3CN), m/z (%): 145 (100) $[PF_6]^-$. Elemental Analysis (%) calculated for $C_{46}H_{47}CuF_6NP_3$ (%): C 62.48, H 5.36, N 1.58; found: 63.23, H 5.10, N 1.96.

In order to study the potential radioprotective effects of copper complexes $[Cu(L^{CF3})_2]$ (complex 1, Figure 1a) and $[Cu(Adm)(PPh_3)_2]PF_6$ (complex 2, Figure 1b) on irradiated organisms, we studied cytogenetic indices in experimental animals (sexually mature male Albino rats, with an average weight of 180-200 g). The animals were divided into 4experimental groups (10 rats in each group):

1. Group I: intact animals.
2. Group II: animals exposed to the radioisotope technetium (Tc), receiving an intraperitoneal injection of the isotope with an activity of 4.8 mCi in a volume of 2 mL ("pure irradiation").
3. Group III: animals intraperitoneally injected with the copper complex $[Cu(L^{CF3})_2]$ at a dose of 50 mg/kg in a volume of 2 mL, administered one hour before the introduction of the Tc isotope ("irradiation + copper compound $[Cu(L^{CF3})_2$, complex 1").
4. Group IV: animals that received the compound $[Cu(Adm)(PPh_3)_2]PF_6$ ("irradiation + copper compound $[Cu(Adm)(PPh_3)_2]PF_6$, complex 2") (dose of 50 mg/kg) before irradiation.

The cytogenetic analysis included chromosome examination using Giemsa staining. Survival rates and cytogenetic parameters were assessed using the Ford-Wollam method [13]. The mitotic index (MI), chromosomal aberrations (CA) and the percentage of polyploid cells (PPC) in the bone marrow cells of the femur were determined by analysing 1000 cells in each preparation.

Data statistical analysis was carried out using a number of specialized statistical packages, including Statsoft and SPSS-10.0. Multiregression and correlation analysis methods were used [14,15].

Results and Discussion.

The survival rate of animals across the 4 experimental groups was evaluated. In the intact or control group ("normal"), survival was 100%. In Group II dropped to 40%. In Group III survival was 90%, and Group IV which was injected with $[Cu(Adm)(PPh_3)_2]PF_6$ before irradiation, maintained a survival rate of 100%. The survival dynamics were described by regression equations:

y_1=100+0*lg(x)
y_2=77,5018-30,38lg(x)
y_3= 104,38-10,53lg(x)
y_4=100+0*lg(x),

where x represents the day of the experiment, y1 is the survival rate of intact animals, y2 is the survival rate under "pure Tc irradiation", y3 is survival rate under "irradiation + $[Cu(L^{CF3})_2]$ injection", and y4 is the survival rate under "irradiation + $[Cu(Adm)(PPh_3)_2]PF_6$ injection".

The above regression equations allow for the extrapolation of survival rate changes percentage at later stages of the experiment, enabling predictions of future outcomes.

By analysing the karyotype and proliferative activity of the studied cells, we obtained the cytogenetic indices for these groups. The results are summarized in Table 1, including only statistically significant changes in cytogenetic indices.

When analysing the results of the study involving the animal groups exposed to "pure irradiation", "irradiation + complex 1" and "irradiation + complex 2", we found significant differences in the cytogenetic indices between these groups. For all 3 indicators, there was a reliable difference between the intact and irradiated animals ($p<0.05$), indicating that these indices can be considered markers of Tc irradiation. For the chromosomal aberrations and the number of polyploid cells, a reliable difference was found in the irradiated animals compared to the group receiving "irradiation + $[Cu(L^{CF3})_2]$" (both after 15 and 30 days), which indicates the radioprotective property of the compound. Regarding the mitotic index (proliferative activity), a tendency toward normalization was observed after 15 days, with a reliable difference between Groups II and III by the end of the study (after 30 days). Survival rates and changes in cytogenetic parameters suggest that $[Cu(L^{CF3})_2]$ is less effective than $[Cu(Adm)(PPh_3)_2]PF_6$. In group IV "irradiation + $[Cu(Adm)(PPh_3)_2]PF_6$", a pronounced and statistically

Table 1. Cytogenetic indices analyzed in 4 groups: "normal (control)", "pure irradiation (Tc exposure only)", "irradiation + $[Cu(L^{CF3})_2]$" and "irradiation + $[Cu(Adm)(PPh_3)_2]PF_6$" on the 15th and 30th days of the experiment.

Indicators	Norm (I Group)	Tc (II Group)	Tc + $[Cu(L^{CF3})_2]$ (III Group) 15 days	Tc + $[Cu(L^{CF3})_2]$ (III Group) 30 days	Tc +$[Cu(Adm)(PPh_3)_2]PF_6$ (IV Group) 15 days	Tc +$[Cu(Adm)(PPh_3)_2]PF_6$ (IV Group) 30 days
MI, %	20.35±2.8	9.8±0.96	11.4±0.16 $0.002<P_{1,3}<0.01$ $P_{2,3}>0.05$	15.8±0.17 $P_{1,3}>0.05$ $P_{2,3}<0.001$	14.8±1.6 $P_{1,4}<0.05$ $0.01<P_{2,4}<0.02$	17.4±1.9 $P_{1,4}<0.05$ $P_{2,4}<0.01$
CA, %	2,6±0,26	6.8±0.74	5.0±0.51 $P_{1,3}<0.001$ $P_{2,3}<0.05$	4.4±0.48 $0.002<P_{1,3}<0.01$ $P_{2,3}<0.05$	4.2±0.52 $0.01<P_{1,4}<0.02$ $0.002<P_{2,4}<0.01$	3.85±0.31 $0.002<P_{1,4}<0.01$ $0.001<P_{2,4}<0.002$
PPC, %	0.5±0.08	4.6±0.53	2.2±0.24 $P_{1,3}<0.001$ $P_{2,3}<0.001$	2.1±0.26 $P_{1,3}<0.001$ $P_{2,3}<0.001$	3.2±0.41 $P_{1,4}<0.001$ $P_{2,4}<0.05$	1.0±0.12 $0.002<P_{2,4}<0.01$ $P_{2,4}<0.001$

$P_{1,3}$, $P_{2,3}$, $P_{1,4}$, $P_{2,4}$ - 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).

significant difference from the "pure irradiation" Group was observed for all 3 parameters starting from day 15.

Figure 2 illustrates the results of multi-regression analysis, showing the mutual influence of cytogenetic indices following the injection of $[Cu(L^{CF3})_2]$ and $[Cu(Adm)(PPh_3)_2]PF_6$. The equations of the multi-regression dependency between MI, CA and PPC in the bone marrow cells of the femur are also provided for the norm (x), pure irradiation (y) and the use of copper complexes (z).

Multi-regression analysis of cytogenetic parameters, along with standard statistical methods, confirmed the highest efficiency of the compound $[Cu(Adm)(PPh_3)_2]PF_6$ compared to $[Cu(L^{CF3})_2]$. This can be seen from the difference in the coefficients of all variables (x, y and z) in the equation. All the $[Cu(Adm)(PPh_3)_2]PF_6$ (complex 2) indicators were higher in absolute values than the $[Cu(L^{CF3})_2]$ (complex 1) indicators.

The following abnormalities were detected during Tc irradiation: double fragments, deletions, polyploidy (Figure 3). The number of these abnormalities was significantly reduced after the administration of complexes 1 and 2, further confirming the beneficial effects of these copper complexes.

Conclusion.

Cytogenetic parameters analysis revealed a significant difference between intact and irradiated animals for all 3 parameters, indicating that these parameters can be considered reliable markers of irradiation with the technetium isotope. Upon evaluating survival and cytogenetic parameters (specifically the mitotic index, chromosomal aberrations, and percentage of polyploid cells in the femoral bone marrow), the highest survival value was observed in the group treated with complex 2 ($[Cu(Adm)(PPh_3)_2]PF_6$). A reliable difference was found in the chromosomal aberrations and the number of polyploid cells in irradiated animals compared to the "irradiation + $[Cu(L^{CF3})_2]$" Group (both after 15 and 30 days), demonstrating the radioprotective properties of the compound. For the mitotic index (proliferative activity), a tendency toward normalization was noted after 15 days in the "irradiation + $[Cu(L^{CF3})_2]$" Group and a reliable difference between Groups II and III by the end of the study (after 30 days), further supporting the beneficial effect of this compound. Analysis of survival rates, changes in cytogenetic parameters, and multi-regression analysis using both complexes confirms the highest efficiency of [Cu(Adm)

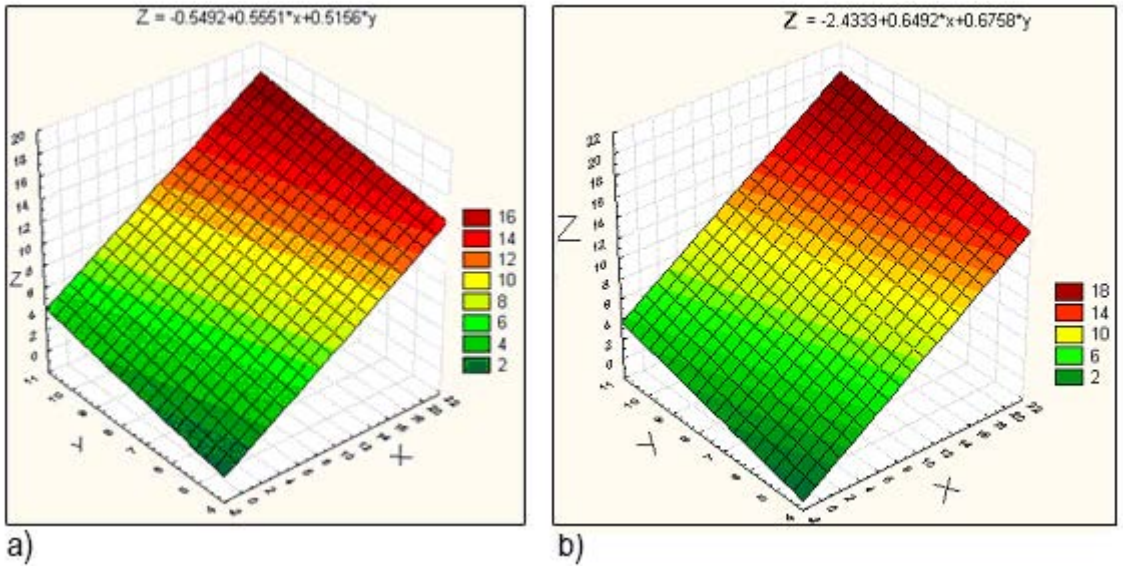

Figure 2. Results of the multi-regression analysis of the interaction between cytogenetic parameters following the injection of $[Cu(L^{CF3})_2]$ (a) and $[Cu(Adm)(PPh_3)_2]PF_6$(b).

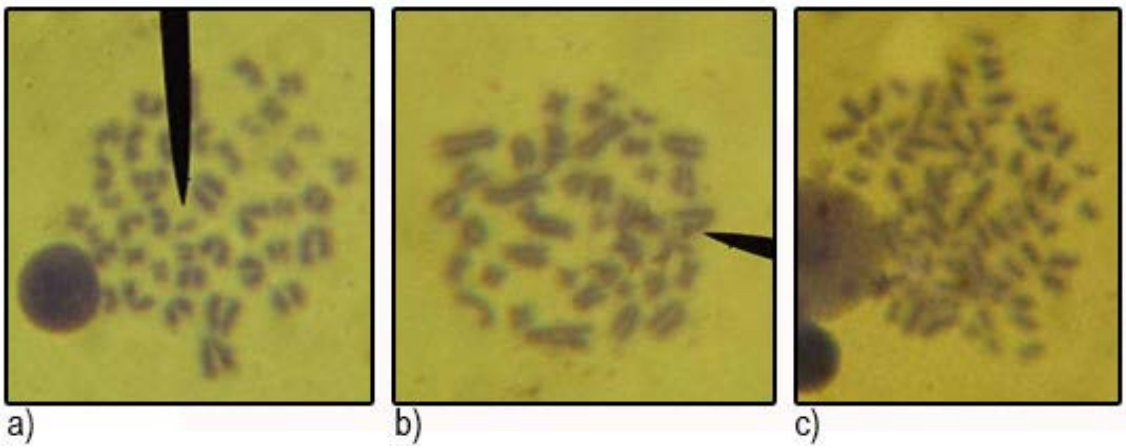

Figure 3. Cytogenetic abnormalities induced by technetium exposure: a) double fragment, b) deletion, c) polyploidy. Magnification: ×900.

$(PPh_3)_2]PF_6$ (complex 2) compared to $[Cu(L^{CF3})_2]$ (complex 1). When using $[Cu(Adm)(PPh_3)_2]PF_6$ in Group IV, a reliable difference from the "pure irradiation" group, was observed across all parameters, with the normalization of cytogenetic parameters from the early stages of observation. This indicates a pronounced radioprotective property of $[Cu(Adm)(PPh_3)_2]PF_6$and an earlier normalization of cytogenetic parameters. The results of this study underscore the importance of continuing research into the development of agents with therapeutic potential for radiation injuries.

Author contributions.

Study Concept and Design: KAG. Acquisition, Analysis, and Interpretation of the Data: KAG, SC, PM, CM, DAM, PZhH, and GVS. SC and PM synthesized the new compounds. KAG, DMH, SC, PM, CM, and GVS wrote the manuscript. All 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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ПРОЯВЛЕНИЕ РАДИОЗАЩИТНЫХ СВОЙСТВ У КОМПЛЕКСОВ МЕДИ $[Cu(L^{CF3})_2]$ И $[Cu(Adm)(PPh_3)_2]PF_6$

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Резюме

Одним из первых и прямых признаков воздействия ионизирующего излучения на клетку является дестабилизация хромосом. При изучении цитогенетических показателей, включая митотический индекс, хромосомные аберрации и количество полиплоидных клеток в клетках костного мозга бедренной кости, была обнаружена значительная разница между интактными и облученными животными. Это говорит о том, что данные показатели можно рассматривать как маркеры облучения изотопом технеция. При оценке выживаемости наибольшее значение выживаемости зафиксировано в группе, получавшей инъекцию $[Cu(Adm)(PPh_3)_2]PF_6$. По показателям

хромосомных аберраций и количеству полиплоидных клеток облученные животные показали достоверную разницу по сравнению с группой «облучение + $[Cu(L^{CF3})_2]$» как через 15, так и через 30 дней после облучения, что свидетельствует о радиозащитном свойстве соединения. Что касается митотического индекса, лечение $[Cu(L^{CF3})_2]$ показало тенденцию к нормализации через 15 дней, с достоверной разницей между группами 2 и 3 к концу исследования (через 30 дней), что дополнительно подтверждает полезный эффект соединения. Анализ выживаемости, изменений цитогенетических показателей и многофакторный регрессионный анализ при использовании обоих комплексов подтверждает наибольшую эффективность $[Cu(Adm)(PPh_3)_2]PF_6$ по сравнению с $[Cu(L^{CF3})_2]$. В частности, лечение $[Cu(Adm)(PPh_3)_2]PF_6$, в отличие от «чистого облучения», привело к достоверной разнице по всем параметрам и привело к нормализации цитогенетических показателей с ранних сроков наблюдения. Это свидетельствует о выраженном радиопротекторном действии соединения и ускоренной нормализации цитогенетических показателей.

Ключевые слова: облучение, митотический индекс, хромосомные аберрации, количество полиплоидных клеток.