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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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No 3 (360) 2025

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IMPLICATIONS OF SYZYGIUM AROMATICUM EXTRACTS TO REDUCE MULTI-DRUG RESISTANCE OF KLEBSIELLA PNEUMONIAE IN INDUCED URINARY TRACT INFECTION OF FEMALE RATS

Mohammed Mosleh Shwaish[1]*, Muhammed Malik Askar[1], Mustafa Adnan Abed Al-Qaysi[1].

[1]Department of Pharmacology and Toxicology, College of Pharmacy, University of Anbar, Iraq.

Abstract.

Numerous studies have reported on the multi-drug resistance of urinary tract infection (UTI)-causing bacteria, thus requiring alternative solutions for this disease. In the past, UTIs were often prevented and cured using medicinal plants. Thus, this study evaluated the potential of *Syzygium aromaticum* or clove extract to mitigate UTI caused by *Klebsiella pneumoniae* using an animal model. In this study, 40 female rats were randomly assigned into five groups, each comprising eight rats: G1(negative control): Healthy, untreated rats; G2(positive control): Rats infected by *K. pneumoniae* and untreated; G3(T1): Rats infected with UTI using *K. pneumoniae* and subjected to 250 mg/kg/day clove extract orally thrice daily; G4(T2): Rats infected with UTI using K. pneumoniae and subjected to 500 mg/kg/day clove extract orally twice daily, and G5(T3): Rats infected with UTI using *K. pneumoniae* and subjected to 750 mg/kg/day clove extract orally once daily. The experiment was carried out for 10 days. Creatinine, urea, and complete blood count (CBC) levels for the G2 group increased significantly ($P \leq 0.01$) compared to G1. Meanwhile, there was a significant decline ($P \leq 0.01$) in all three parameters for the T1, T2, and T3 groups. Nonetheless, most parameters in the treatment groups returned to normal levels after 10 days of therapy and were comparable to G2. The scanning electron microscopy (SEM) images demonstrated the distinctive effect of *S. aromaticum* on *K. pneumoniae* infection, characterised by a rough or wrinkled cell surface, deep pores, altered shape, cavitations, and cracks with the leaking of intracellular contents. In summary, this study demonstrated the potential of the hydroethanolic clove extract at different doses and intervals as a promising alternative solution to reduce bacterial resistance, which was primarily due to the safety of active ingredients in the phytochemical extract.

Key words. Urinary Tract Infection (UTI), histopathological changes, scanning electron microscopy, VITEK® 2 system, *Syzygium aromaticum, Klebsiella pneumoniae*, plant extract.

Introduction.

Herbal medicine refers to the use of extracts from various plant parts as prophylaxis and therapeutics for disease control. The World Health Organisation (WHO) reported that more than 80% of healthcare needs in developing countries are met through the utilisation of herbal medicine as an alternative therapy [1,2]. Numerous empirical studies have proven the pharmacological properties of herbal plants, including anti-inflammatory, antimicrobial, antioxidant, analgesic, bactericidal, fungicidal, spasmolytic, sedative, local anaesthetic, virucidal, embalmment, and food preservation [3] .Phytoconstituents found in plant extracts, including terpenes, tannins, saponins, steroids, alkaloids, glycosides, and flavonoids, are responsible for their beneficial properties [4]. More than 10,000 species of known and classified terrestrial plants have medical applications [5], including as a cure and prevention of urinary tract infections (UTIs).

Plant extracts have demonstrated antimicrobial activities with fewer reported side effects compared to synthetic drugs [6]. The antifungal, antiviral, antibacterial, and anticarcinogenic abilities of fragrant herbs such as thyme, cinnamon, mint, oregano, and clove (*Syzygium aromaticum*, syn., *Eugenia aromaticum* or *Eugenia caryophyllata*) are well-documented, particularly the essential oils (EOs) [7]. Despite that, clove has been under the spotlight more than other spices due to its richness in phenolic compounds. The clove tree is native to east Indonesia and belongs to the family *Myrtaceae*. Clove is known for its potent antiparasitic, antimicrobial, anti-ulcerogenic, anti-thrombotic, anti-inflammatory, and antioxidant properties [8,9]. Literature has reported the use of this aromatic dried flower in Western botanical medicine and Chinese traditional medicine [10]. In dentistry, clove EO is used for emergency cases [11].

One of the major phenolic compounds in clove is eugenol and its derivatives, which demonstrate antioxidant, anticancer, anti-inflammatory, antimicrobial, antiviral, anti-nociceptive, wound healing and insecticidal activities [12,13]. This phenylpropanoid compound is also found in *Cinnamomum* spp., *Origanum vulgare*, *P. nigrum*, *S. aromaticum* L., *T. vulgaris,* and *Zingiber officinale* [14]. A phenylpropanoid derivative of eugenol known as eugenyl acetate also exhibits antiviral, antimutagenic, antibacterial, anticancer, and antioxidant properties [15]. Another bioactive compound present in clove is β-Caryophyllene, which is soluble in organic solvents such as ethanol but exhibits poor solubility in water. This sesquiterpene demonstrated anticancer properties against leukaemia, lymphatic, pancreatic, breast, skin, cervical, and prostate cancer, besides exhibiting local anaesthetic, antioxidant, anticarcinogenic, anxiolytic-like, anti-inflammatory, and antimicrobial properties [16].

The UTI is caused by various microorganisms (uropathogens), including bacteria, fungi, and viruses. Nevertheless, 95% of UTI cases in humans are caused by bacteria [17], particularly *Klebsiella pneumoniae* [18]. This bacterium also causes UTIs in animals [19]. Numerous diseases are triggered by UTIs, such as acute, chronic, and recurrent infections and asymptomatic/symptomatic bacteriuria [20]. Over the years, there have been increasing reports of antibiotic resistance against these UTI-causing bacteria in developing and developed countries. This situation poses a global threat, particularly for the widely used beta-lactam antibiotics. Beta-lactamase enzymes [metallo-beta-lactamases, AmpC beta-lactamase, extended-spectrum beta-lactamase (ESBL) (MBLs)] have been identified as the primary cause of antibiotic resistance [21,22], posing therapeutic

challenges due to the limited treatments for UTIs. Thus, researchers continue their efforts to develop novel solutions to mitigate this illness [23]. The current study investigated the ability of clove extract as an antimicrobial agent to inhibit *K. pneumoniae in rats with* UTI. This study also observed the effects of clove extract in minimising side effects and the impacts on serobiochemical and blood indices of the infected female rats.

Materials and Methods.

Plant extract preparation:

Clove buds were obtained from a local market in Ramadi City, Iraq. Subsequently, the specimens were identified by the personnel in charge of the herbarium in the College of Science, University of Baghdad. Once the specimen had been confirmed, the extraction process was carried out using an organic solvent, 70% hydroalcoholic ethanol. Firstly, the clove buds were rinsed thoroughly and sterilised with distilled water before drying. The dried cloves were then ground using a mechanical mortar and put into powder form. In the next step, the homogenised clove powder (150 g) was poured into hydroalcoholic ethanol (500 ml). The mixture was incubated with a 25-cover magnetic stirrer. After 48 h, the mixture was centrifuged for 10 mins at 5000 rpm, and clear filtrates were obtained after filtration using a Whatman filter paper. The remaining biomass was discarded. The next step involved the concentration of extracts using the rotary evaporator (MRC -UK), which was later stored at 4°C until the subsequent experiment. The extract yield was determined by Zaidiyah et al. [24] as follows:

Extract yield (%) = (R/S) *100

Where:

R: Weight of extract residue; S: Weight of raw sample

Bacteriological examination.

Bacterial isolates and identification:

Bacterial isolates were taken from hospitalized patients and those with MDR characteristics were identified and selected for the article that had been diagnosed from UTI via routine methods and using the VITEK® 2 Compact B system (bioMérieux, French) were identified from urine samples that collected. Selective isolate was also tested for ESBL production using NO45 cards for the VITEK®2 Compact B System. The VITEK®2 Compact B System is an automated microbial identification system that can be used for the metallo beta-lacta-mases detection. The isolates were classified as MDR based on established guidelines. The data were analyzed using Clinical and Laboratory Standards Institute (CLSI) breakpoints [25]. This step was carried out in the laboratory of Al-Ramadi Teaching Hospital for Women and Children, Iraq. The identification occurs by an overnight subculture of suspected *K. pneumoniae* colonies was suspended in 2.5 ml of 0.45% NaCl to prepare 1.5×10^8 CFU/ml (0.5 McFarland) bacterial suspension in a 12 × 75 mm clear polystyrene test tube. The bacterial density was adjusted with the aid of a densitometer (Densicheck®, Biomerieux). The prepared bacterial suspension was loaded into the VITEK® 2 system by Gram-negative rods card (GNR) to read the kinetic fluorescence measurements. The results were obtained within 3 h [26]. The *K. pneumoniae* pure culture was streaked on the brain heart infusion slant before being incubated for 24 h at 37ºC. The number of Gram-negative *K. pneumoniae* isolates growing on the media should exceed the weak or dead bacterial population to indicate that the bacterial culture has entered the log phase [27].

Experimental design:

The animal study was conducted in a laboratory at the Department of Physiology and Pharmacology, College of Veterinary Medicine, University of Fallujah, Iraq. Firstly, 40 female rats were randomly assigned into five groups, each comprising eight rats. The rat age ranged between 10–12 weeks, and their weight was between 250 and 280 g. The rats were handled with care to avoid unnecessary stress. All rats were examined to ensure that they were healthy and disease-free.

Group 1 (Negative control): Healthy rats.

Group 2 (Positive control): Rats infected with UTI using K. pneumoniae without treatment.

Group 3 (T1): Rats infected with UTI using K. pneumoniae and subjected to 250 mg/kg/day clove extract orally thrice daily for 10 days.

Group 4 (T2): Rats infected with UTI using K. pneumoniae and subjected to 500 mg/kg/day clove extract orally twice daily for 10 days.

Group 5 (T3): Rats infected with UTI using K. pneumoniae and subjected to 750 mg/kg/day clove extract orally once daily for 10 days.

Ethical Approve:

According to the proposals, recommendations and approval of this committee, were approved by Veterinary Medicine College \ Scientific Research Ethical Committee in Fallujah, Iraq gave permission for the study methods involving lab animals' rats (approval number 2, dated 23-3-2024).

Haematological methods for complete blood count (CBC):

At the end of the experiment, whole blood samples were collected from each rat and placed in ethylenediaminetetraacetic acid (EDTA) anticoagulant tubes (AFCO, Jordan). The blood samples were subjected to haematological analysis using the automated haematology analyser, and the settings were changed to rat samples. The haematological parameters analysed include packed cell volume (PCV), red blood cells (RBCs), white blood cells (WBCs) and differential WBCs count, and mean corpuscular volume (MCV).

Serobiochemical methods:

Blood samples collected from each rat before, during, and after the treatment period were allowed to clot, which were later centrifuged (Hettich, Germany) for 5 min to obtain the sera. The sera samples were placed in a -20°C freezer until use. The enzyme activity assessment was conducted following the instructions of the Roche Diagnostic Hitachi 902 Analyser (Germany, 2019). The data obtained from this analysis include urea and creatinine data.

Statistical assessment:

The Statistical Analysis System- SAS (2018) program was used to detect the effect of difference factors in study parameters, the

probability mean was measured as $P < 0.01$ significance; Least significant difference-LSD was used to significant compare between means (ANOVA/ one and two way) in this study.

Results.

Clove (*S. aromaticum) extract:*

Hydroalcoholic ethanol has a higher polarity (5.2) than other organic solvents [petroleum ether (0.1), dichloromethane (3.1), acetone (5.1) [28], thus selected as the organic solvent to extract active phytochemicals from cloves in the present study.

The resulting clove extract had a reddish-brown appearance with a yield of 20%, as shown in Figure (1). The yield of extract was calculated as recommended by Zaidiyah et al. [24].

Figure 1. *Extraction of Syzygium aromaticum using hydroalcoholic ethanol yielded reddish-brown powder.*

Yield of extract (%) = Weight of extract (g) / Weight of *S. aromaticum* (g) × 100

= 30 g / 150 g × 100

= 20%

The yield obtained in this study was slightly higher than a study conducted by Tanko et al. [29], which recorded a recovery extract yield of 18.2 % (w/w).

Bacteriological examination

Induction of experimental infection:

The *K. pneumoniae* infection was performed following Zykov (2020) with modifications. A volume of 0.1 ml (2.6×10^6) CFU/ml bacteria suspension was inoculated through the rat's extra urethral orifice once (1.0 cm into the urethra), as shown in Figure 2.

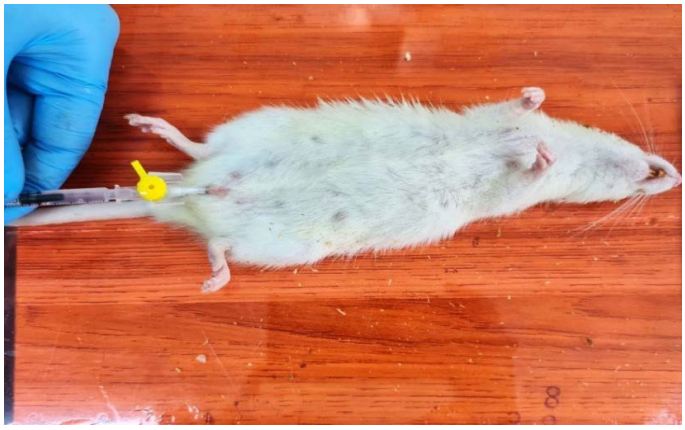

Figure 2. *K. pneumoniae infection induced through the rat's urethral orifice.*

Bacteria identification via VITEK® 2 compact system:

The mechanistic, fluorescence-based VITEK® 2 compact system is used for accurate and rapid identification of clinically important bacteria isolates [30]. Table 1 presents the results obtained from this analysis. The system confirmed the presence of *K. pneumoniae* through the spectrophotometric reading, particularly the bacterial–substrates biochemical reactions (loaded to the Gram-negative card). The isolates achieved an excellent identification level with a probability of 91% based on the technical datasheet. Furthermore, the results were consistent with an earlier study by Al-Baer and Hussien [31] where the isolated *K. pneumoniae* was 90 % similar to the *K. pneumoniae* in the standard Gram-negative card. A highly accurate detection method is crucial in the clinical field to confirm the predominant bacterial isolate that causes the disease and determine the course of action or antibacterial agent to treat the UTI [32]. According to Liu *et al*., [33] the decreased food consumption among UTI patients was linked to *K. pneumoniae lipopolysaccharide* (LPS), which triggers acute bacterial infection symptoms such as fever and anorexia. Moreover, this endotoxin alters the morphology of the digestive tract, such as the intestines, thus reducing food intake. Therefore, anorexia during infection potentially aims to limit nutrient availability that fuels pathogenic organism development. ESBL generation was found in this isolate based on their susceptibility to various antibiotics. Every strain known to produce ESBL is multidrug resistant (MDR) [34].

Evaluation of CBC values of female rats:

Table (2) presents the CBC results after the statistical analysis. The WBC and neutrophil levels of rats in the T1 and T2 groups returned to normal post-treatment, and the values were comparable to the healthy rats (G1 group). Meanwhile, there were significant increases ($P < 0.01$) in all infected groups 2 (positive control group). A statistically significant difference ($P < 0.01$) were also observed in RBC, MVC levels between the G2 and T1 groups, which did not return to normal levels at the end of the experiment. Conversely, the RBC, MCV levels of T2 and T3 returned to normal after the 10-day treatment, and the value were comparable to that of healthy rats (G1 group). Meanwhile, PCV levels between T1, T2, and T3 groups did not exhibit significant differences ($p > 0.01$). There WBC, Neutrophil and were a significant decrease ($P < 0.01$) for the treatment groups T1, T2, and T3 for the cohorts compared to the G2 groups and reach to the normal value such in G1.

Determination of serum creatinine concentration (mg/dl)

Table 3 presents the mean serum creatinine values of female rats after 10 days. The serum creatinine concentrations of all animals were similar ($p > 0.01$) and within the normal range before the infection, indicating their good health status. Serum creatinine levels of G2 (0.48 mg/dl), T1 (0.49 mg/dl), T2 (0.47 mg/dl) and T3 (0.48 mg/dl) groups were significantly different ($P < 0.01$ from G1 (0.27 mg/dl) group (negative control) after two days of infection. The mean creatinine values in the T2 (0.35 mg/dl) and T3 (0.32 mg/dl) groups decreased after five days and returned to normal without significant difference ($p > 0.01$) with the G1 group (0.27 mg/dl). Conversely, the creatine levels were significantly different ($p > 0.01$) between T2 and T3 groups from

Table 1. *VITEK® 2 system results for the biochemical reactions and sensitivity test of K. pneumoniae samples.*

Identification information			**Analysis time:** 4.83 h		**Status:** Final
Selected organism			91% probability ***Klebsiella pneumoniae*** **Bionumber** 0405610670526210		
ID analysis messages					
Susceptibility information	**Analysis Time:** 8.73 hours				**Status:** Final
Antimicrobial	**MIC**	**Interpretation**	**Antimicrobial**	**MIC**	**Interpretation**
Ticarcillin	≥ 128	R	Amikacin	16	*I
Ticarcillin/ Clavulanic acid	≥ 128	R	Gentamicin	8	I
Piperacillin	≥ 128	R	Tobramycin	≥ 16	R
Piperacillin/ Tazobactam	16	S	Ciprofloxacin	≥ 4	R
Ceftazidime	16	R	Pefloxacin		
Cefepime	≥ 64	R	Minocycline	≤ 0.5	S
Aztreonam	≥ 64	R	Colistin		
Imipenem	≤ 25	S	Rifampicin		
Meropenem	≤ 25	S	Trimethoprim/Sulfamethoxazole	≥ 320	R

Advanced Expert System (AES); minimum inhibitory concentrations (MIC); S: sensitive; R: resistant; iR: intermediate resistant.

Table 2. *The CBC values of female rats infected with K. pneumoniae.*

Groups	**WBC**	**Neutrophil**	**RBC**	**MCV**	**PCV**
Group 1 **Negative control**	25.75 ± 3.23 AB	7.62 ± 0.076 B	9.72 ± 0.69 A	59.75 ± 0.85 A	44.25 ± 2.05 BC
Group 2 **Positive control**	37.65 ± 1.22 A	10.37 ± 0.33 A	5.10 ± 7.59 C	36.75 ± 0.25 C	56.0 ± 2.16 A
Group 3 (T1) 250 mg/2ml/Thrice daily orally	28.22 ± 8.12 AB	7.35 ± 0.86 B	8.87 ± 0.27 B	53.07 ± 0.04 B	48.0 ± 0.47 B
Group 4 (T2) 500 mg/2ml/Twice daily orally	26.3 ± 0.07 AB	8.01 ± 0.07 B	9.95 ± 0.21 A	58.9 ± 0.37 A	40.01 ± 0.38 BC
Group 5 (T3) 750 mg/2ml/Once daily orally	25.2 ± 0.04 AB	7.91 ± 0.05 B	9.68 ± 0.34 A	57.5 ± 0.22 A	42.06 ± 0.17 BC
LSD	**5.62**	**2.03**	**1.01**	**2.62**	**9.12**

- Values represent mean ± standard error (SE).
- Means with different capital letters in the same column are significantly different.
*- * (P ≤ 0.01).*
- White blood cells (WBC), red blood cells (RBC), mean corpuscular volume (MCV), packed cell volume (PCV), east significant difference (LSD) least significant difference.

Table 3. *Serum creatinine levels of female rats infected with UTI using K. pneumoniae and administered orally with S. aromatic (clove) extracts at different doses for 10 days.*

Groups	**Creatinine (mg/dl) Mean ± SE**			
	Period			
	Before infection	**After 2 days of UTIinduction**	**After 5 days of treatment**	**After 10 days of treatment**
Group 1 **Negative control**	0.29 ± 0.05 A a	0.27 ± 0.04 C a	0.27 ± 0.03 C a	0.28 ± 0.04 B a
Group 2 **Positive control**	0.28 ± 0.03 A c	0.48± 0.07 B a	0.64 ± 0.07 A ab	0.89 ± 0.08 A a
Group 3 (T1) 250 mg/2ml/Thrice daily orally	0.27 ± 0.02 A c	0.49 ± 0.05 B a	0.40 ± 0.05 B ab	0.31 ± 0.04 B a
Group 4 (T2) 500 mg/2ml/Twice daily orally	0.28 ± 0.04 A b	0.47 ± 0.04 B a	0.35 ± 0.03 B ab	0.29 ± 0.03 B b
Group 5 (T3) 750 mg/2ml/Once daily orally	0.28 ± 0.06 A b	0.48 ± 0.03 B a	0.32 ± 0.02 B b	0.25 ± 0.06 B b
LSD value	**0.135**			

- Values represent mean ± SE
- Means with different capital letters in the same column and small letters in the same row are significantly different.
*- *(P ≤ 0.01).*
- Urinary tract infection (UTI); least significant difference ((LSD)).

Table 4. *Serum urea concentration (mg/dl) of female rats infected with K. pneumoniae.*

Groups	Urea (mg/dl) Mean ± SE			
	Period			
	Before infection	After 2 days of UTI induction	After 5 days of treatment	After 10 days of treatment
Group 1 **Negative control**	27.01 ± 1.73 A a	26.91 ± 1.33 C a	25.92 ± 1.73 C a	26.45 ± 1.05 C a
Group 2 **Positive control**	25.33 ± 1.08 A d	42.45 ± 2.27 A c	53.10 ± 1.08 A b	70.27 ± 3.06 A a
Group 3 (T1) 250 mg/2ml/Thrice daily orally	27.47 ± 1.07 A b	44.06 ± 2.52 A a	40.45 ± 1.42 B a	35.15 ± 1.76 B a
Group 4 (T2) 500 mg/2ml/Twice daily orally	26.79 ± 1.42 A c	43.12 ± 1.97 A a	32.88 ± 1.66 C b	29.87 ± 1.20 C c
Group 5 (T3) 750 mg/2ml/Once daily orally	25.87 ± 1.42 A c	42.30 ± 0.99 A a	30.81 ± 1.66 C b	25.36 ± 1.20 C c
LSD value	2.15			

- Values represent mean ± SE.
- Means with different capital letters in the same column and small letters in the same row are significantly different.
- *($P \leq 0.01$).
- Urinary tract infection (UTI); least significant difference (LSD).

the G2 group. At the end of the experiment, the T2 (0.29 mg/dl) and T3 (0.25 mg/dl) groups exhibited a further reduction in creatinine concentration from the G1 (negative control) group, but without significant difference ($p > 0.01$). Conversely, the T2 and T3 groups' creatinine levels were significantly different from the G2 (positive control) group after 10 days.

Determination of serum urea concentration (mg/dl):

Table 4 demonstrates the mean values of serum blood urea concentration in female rats. The blood serum urea concentration in each group was within the normal range before the infection, without significant differences ($p > 0.01$) between groups. At two days post-infection, the levels of blood serum urea in all UTI rats increased significantly ($P < 0.01$) except in the negative control group. The serum urea values of T1 (40.45 mg/dl), T2 (32.88 mg/dl), and T3 (0.33 mg/dl) groups decreased significantly ($P < 0.01$) compared to G1 and did not return to normal after five days of treatment. Nevertheless, the serum urea levels decreased significantly ($P < 0.01$) after 10 days of treatment in T2 (32.88 to 29.87 mg/dl), and T3 (30.81 to 25.36 mg/dl) groups compared with healthy rats (G1 group) (26.45 mg/dl) and returned to the normal range. In contrast, the T1 group serum urea levels did not return to normal levels after 10 days of treatment. Meanwhile, the serum urea concentration of infected and untreated rats (G2 group) was 70.27 mg/dl and continued to increase compared to the rest of the groups.

Clinical signs:

Before the infection was introduced, all rats were healthy, with normal faeces and yellow urine. At two days post-infection, the UTI rats were anorexic, dehydrated, and the colour of their urine was dark yellow. After three days of infection, abnormally frequent urination began to increase gradually. The urine of infected rats was also foul-smelling and cloudy. Behavioural changes were evident **in** T2 and T3 groups **after** day 5 of treatment, exhibiting faster recovery and compering. These changes were less apparent in the T1 group. The clinical signs improved recovery and returned to normal after 10 days of treatment for treated groups, particularly in the T2 and T3 groups.

SEM results:

The SEM results demonstrated that the *K. pneumoniae* in the positive control group (G2) were clustered and appeared normal in size, short and rod-shaped. In contrast, bacterial cells treated with 100 mg/kg clove extract (T1 group) were elongated with particles observed around their surfaces. The cells appeared rough and filamentous on their surfaces, with intracellular contents leaking out (Figures 3 and 4). The *K. pneumoniae* cells in the T2 and T3 groups appeared crumpled with grooves and deep pores on the cell surface. The bacterial cell division was also abnormal. Furthermore, the cell membrane was also damaged, indicated by loosened cell walls, shrinkage, and convoluted surfaces (Figures 5 and 6).

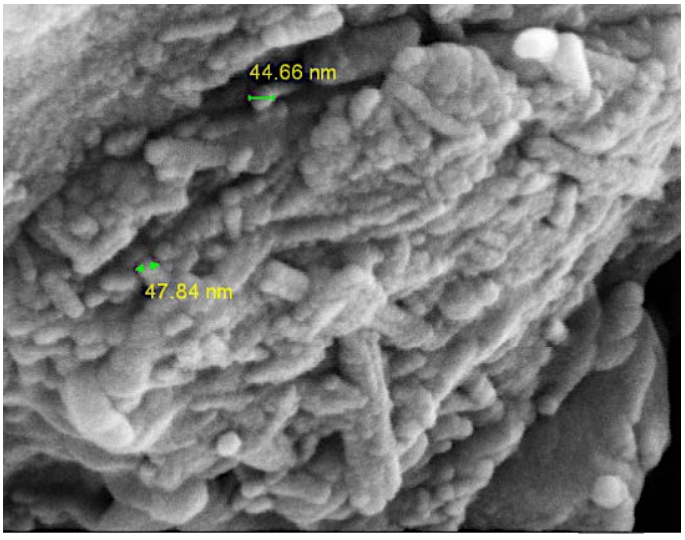

Figure 3. *The SEM image for the positive control group (G2) showed K. pneumoniae cells as clustered, rod-shaped, and normal in size with smooth and intact cell surfaces.*

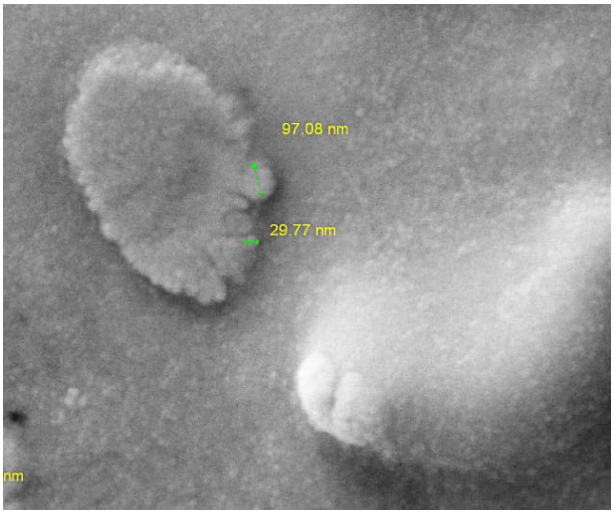

Figure 4. *The SEM image demonstrates the effect of S. aromaticum on K. pneumoniae in the T1 group. The bacterial cell was elongated and deformed with rough surfaces, and the intracellular contents leaked out.*

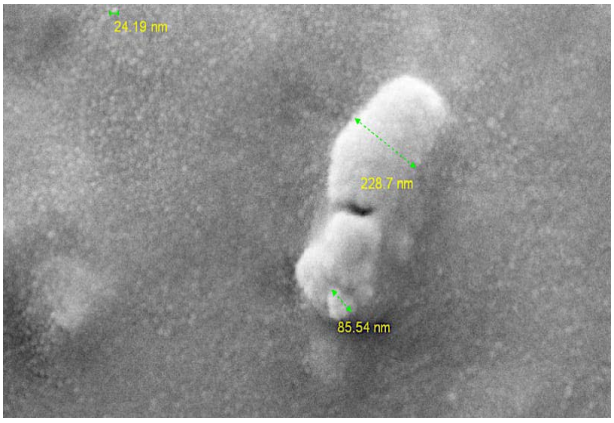

Figure 5. *The SEM image illustrates the effect of S. aromaticum on K. pneumoniae in the T2 group. The bacterial cell was deformed and altered with extensive cellular debris, decomposition of inner organelles on cell surfaces, and the leaking out of intracellular contents.*

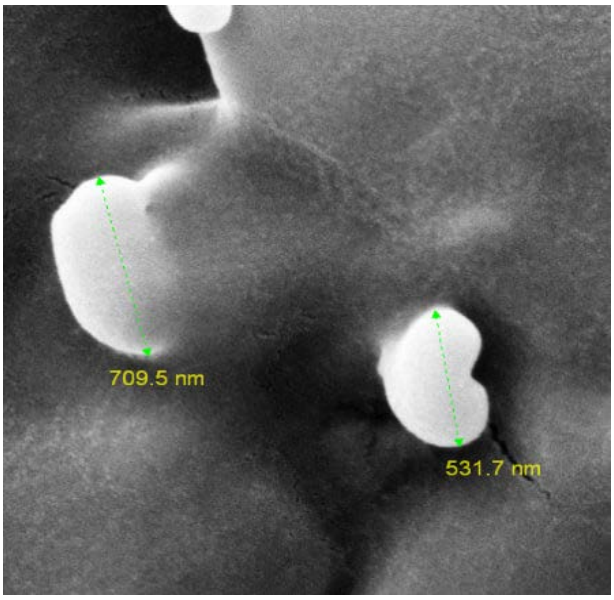

Figure 6. *The SEM image illustrates the effect of S. aromaticum on K. pneumoniae in the T3 group. The bacterial cells had rough or wrinkled cell surfaces, deep pores, altered shape, cavitations and cracks with intracellular contents leaking out.*

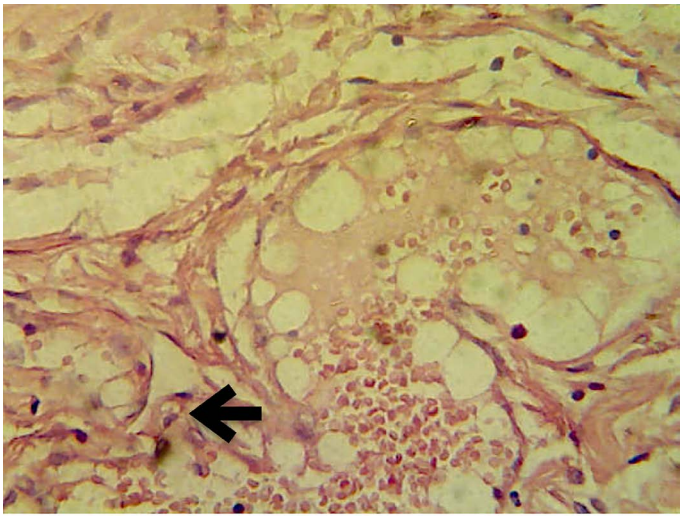

Figure 7. *A section of the bladder of from the untreated rat (positive control group). The image shows moderate inflammatory cell infiltration around and in congested blood vessels (arrow)(H & E stain, 40 × magnification).*

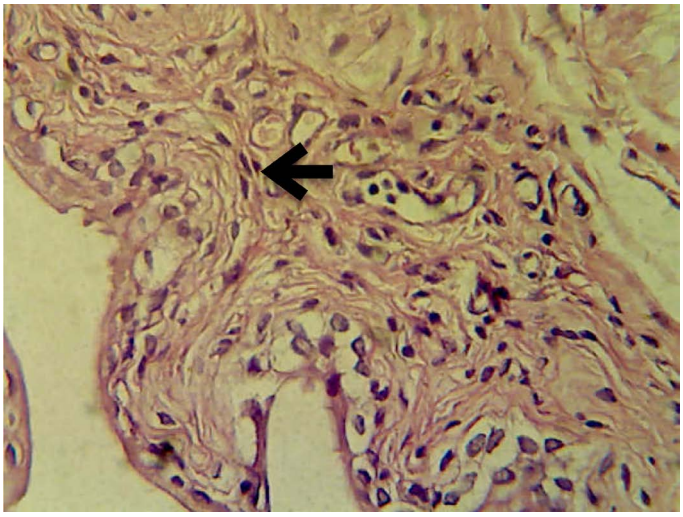

Figure 8. *A section of the urinary bladder of rat (T1 group). The image demonstrates moderate inflammatory cell infiltration between the muscular layer (arrow)(H & E stain, 40 × magnification).*

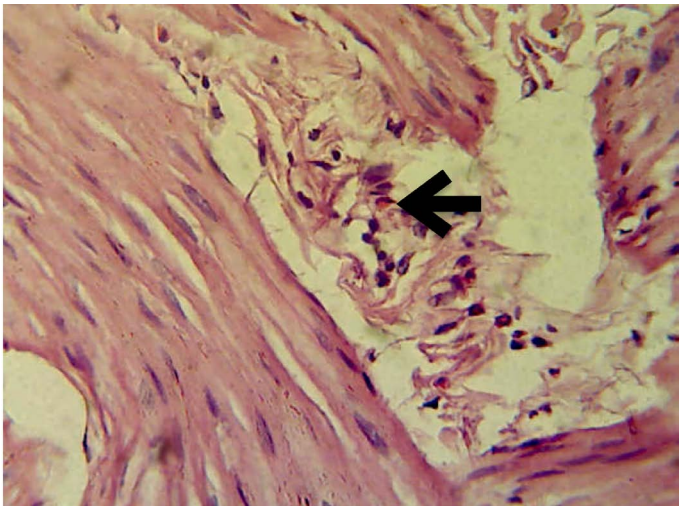

Figure 9. *A section of the urinary bladder of the T2 group. The image illustrates moderate inflammatory cell infiltration between muscle fibre (H & E stain, 40 × magnification).*

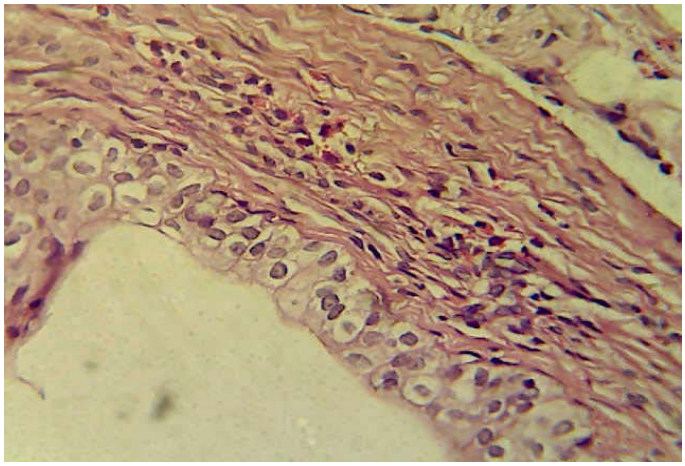

Figure 10. *A section of the urinary bladder of rats in the T3 group. The image indicates no clear lesion (H & E stain, 40 × magnification)*

Discussion.

Bacterial resistance to chemical antibiotics continues to rise, posing a threat to human and veterinary health globally. Thus, researchers continue their search for alternative solutions to eradicate resistant microbial strains [35]. One of the most promising avenues to mitigate bacterial resistance or to create synergistic effects with antimicrobial drugs is phytotherapy and herbal medicine [36]. It is common for *Klebsiella pneumoniae* to show resistance to β-lactam drugs and from one of the most important explanations I found is what the researchers mentioned in their article, and I went to the same explanation and the same direction regarding selected isolation. The formation of β-lactamases, the most important of which are cephalosporinases, including carbapenemases and extended-spectrum β-lactamases, is the main way that this resistance is shown [37]. The rise of multi-drug-resistant bacteria has been correlated with four resistance mechanisms that bacteria use to lessen the effects of antibiotics [33]. Antibiotic enzyme modification and deactivation are the basis for the first; restricted access to drug targets is the basis for the second; drug target alteration or perhaps target extinction is the basis for the third; and physical resistance is the basis for the fourth [38]. Despite the bacteria's considerable amount of antibiotic resistance, the isolate of the bacteria in this study was shown to be positive for extended-spectrum beta-lactamases [34]. This suggests that distinct resistance pathways may be present in the remaining isolates. So, it was used, and the idea is how to get rid of resistance using cloves because of its distinctive components to get rid of bacterial resistance.

Earlier studies have reported the potential of clove extract to inhibit broad-spectrum pathogen activity. The antibacterial mechanism of this herbal plant is linked to the meta and ortho hydroxyl (-OH) groups in the chemical structure, which possess the ability to alter the microbial cell's cytoplasmic membrane [39-41].

Studies have shown that clove EO can inhibit Gram-positive bacteria (*L. monocytogenes*, *S. aureus*, *Streptococcus*), Gram-negative bacteria (*Agrobacterium*, *Pseudomonas aeruginosa, Erwinia carotovora*, *K. pneumoniae, Salmonella*), yeast [39-41] and fungi (*Aspergillus flavus*, *A. parasiticus*, *A. ochraceus*, *Penicillium*, *C. albicans*).

Eugenol, the main component of clove (*Syzygium aromaticum*), is a powerful bioactive ingredient that makes it a popular therapeutic plant. Eugenol, along with other components including β-caryophyllene and eugenyl acetate, has a significant impact on the pharmacokinetics and pharmacodynamics of clove extract [4].By the gastrointestinal system absorbs eugenol quickly. This supports and agrees with what we found in group T2, which was more suitable and exactly pharmacologically in group T3. Peak plasma levels of Eugenol are usually reaching rapidly plasma and blood with mean half-lives of 14.0 h and 18.3 h, respectively after oral dosing so that after repeated daily dosages, a cumulative effect has been proposed and linked to the reduction of pain and inflammation; Eugenol's lipophilia contributes to it being easier for biological membranes to absorb it [42,43]. Eugenol is widely distributed throughout bodily tissues, such as the liver, kidneys, and central nervous system, as a result of its lipophilicity. It has analgesic and anesthetic effects because it easily passes the blood-brain barrier and excreted by kidney [44].

The lipophilic properties of clove EO can permeate cell membranes and interact with phospholipids, fatty acids, and polysaccharides. This mechanism of action results in cell death due to the leaking out of cellular contents, proton pump disruption, and compromised structural integrity of the cellular membrane. Furthermore, cloves extract demonstrated anti-inflammatory activities, inhibiting tissue remodelling and pro-inflammatory protein expression such as cytokines, cyclooxygenase (COX-2), nuclear factor kappa B (NF-kB), prostaglandin synthesis and neutrophil chemotaxis, besides suppressing inflammatory biomarkers [45-47].

This study investigated the potential of clove extract as a substitute for conventional antibiotics against UTIs. It is generally accepted that clove and its essential oil is safe to take at levels below 1,500 mg/kg. However, according to the World Health Organization (WHO), humans can consume 2.5 mg of cloves per kilogram of body weight each day [48]. The dosages of the hydroethanolic clove extract used in this study were chosen based on earlier findings in an in vitro experiment, which demonstrated positive results in the current animal study post-infection and treatment. For instance, the CBC analysis showed that female rats infected by *K. pneumoniae* and treated with clove extracts at various doses improved in most parameters, where some values were better than the healthy rats (G1 group) One of the most important things mentioned and will be explained is what we have reached in our article, especially with regard to the treatment of RBC MCV and for the T1 group and comparing it with T2 ,T3 and G1, which is what one of the researchers explained that the effects of acute and chronic damage to the kidneys in rats were examined in a study conducted by Garrido et al. [49]. When compared to control groups (G2), the results showed that rats with renal injury had significantly lower and red blood cell (RBC) counts and MCV. Elevated hepcidin levels, which can prevent iron availability for erythropoiesis, and abnormalities in iron metabolism were linked to this anemia. Furthermore, Urea and creatinine are essential laboratory indicators for evaluating renal function and may offer indirect indications of urinary tract infections (UTIs) and their possible advancement to renal

involvement [50,51]. Urea and creatinine levels in the T2 and T3 groups returned to the normal range after 10 days of treatment, and the values were comparable with the healthy rats (G1 group). Similarly, Haro-González *et al*. [43] reported that clove extract exhibited antimicrobial effects by destabilizing the integrity and permeability of the cell membrane, rupturing the phospholipid membrane, and inhibiting cell growth. These mechanisms eventually led to cell death caused by disruption in enzymatic activities, protein translocation, electron transport, and phosphorylation.

The SEM observation aligns with the findings of Justice *et al.* [52], where bacterial filamentation is deemed a survival mechanism of bacterial cells to maintain morphological plasticity under stress. As a similar observation was reported in a study using cinnamon bark EO against pathogenic *Porphyromonas gingivalis*, with clear damage to the membrane integrity and cell permeability [53].

Earlier studies have reported the efficacy of clove oil obtained from different extraction methods against *K. pneumoniae* [54,55], yielding similar results to the current study. Clove oil administration promoted antimicrobial activity against organisms without depressing the lysozyme activities or the mammalian innate immunity [56]. In the present study, clove-treated groups experienced a surge in lysozyme activity and nitric oxide, potentially due to enhanced innate immunity. Activated macrophages and neutrophils contain inducible nitric oxide synthases (iNOS) to generate nitric oxide in abundance when the host is under immunological duress [57,58]. In addition, phagocytes synthesise reactive oxygen and nitrogen species to neutralise the invading organisms [59] to boost the host's defence mechanism.

Hydroalcoholic clove extract potentially possesses bioactive compounds that can destroy or hinder WBC production by either inhibiting regulatory factor synthesis, impairing stem cell sensitivity or eliminating WBC directly [10,60]. A study reported that rats with UTI caused by *K. pneumoniae* developed early clinical signs such as appetite loss, fever, foul-smelling and cloudy urine, and the inability to rise body in less than 24–48 h [61]. Anorexia is also a common occurrence in infection, implying that this condition may be an integral component of the acute phase response that influences negative nitrogen balance and weight loss [62]. This hypothesis was proven when rats inoculated with *K. pneumoniae* endotoxin exhibited reduced food consumption and elevated body temperature [63]. In the present study, the clove-treated groups returned to their normal condition after 10 days. Conversely, rats in the positive control group became dehydrated due to frequent urination, loss of skin elasticity, weight loss, thinness, laboured breathing, and coarse fur, which aligned with previous findings [64].

The rat's bladder tissues were examined microscopically for morphological changes caused by pathogenic *K. pneumoniae*. The histopathological examination of the G2 group (positive control) indicated changes in the renal corpuscular components and more dilatation in the Bowman's spaces. This lesion appears in the highly severe and advanced stage of infection, characterised by the severe infiltration of inflammatory cells around and in congested blood vessels (Figure 7). Likewise, Joshua *et al*. [65] revealed that *K. pneumoniae* and *E. coli* are major causes of hemolytic uremic syndrome that affects all ages. This renal disease is associated with severe UTI, cystitis, and pyelonephritis. Meanwhile, infected rats that received 250 mg/2 ml clove extract thrice daily for 10 days exhibited congested and dilated blood vessels. The presence of oedema and mild infiltration of inflammatory cells between muscle fibres were also evident in this group (Figure 8). This observation is similar to those reported by Samir and Orooba [66], which included infiltration of inflammatory cells, tubular dilatation, Bowman's space dilation, necrosis, and congestion. These results may be attributable to renal injury in the kidney due to bacterial endotoxin production and incomplete eradication of ciprofloxacin against pathogenic bacteria [67].

The histopathological findings of rats treated with 500mg/2ml twice daily of extract for 10 days indicated improved inflammation and less severe histopathological changes with mild inflammatory cell infiltration between renal tubules (Figure 9). Meanwhile, the bladder morphology of rats treated with 750mg/2ml cove extract once daily for 10 days had no clear lesions and resembled that of healthy rats (negative control) (Figure 10). The inhibition of lipopolysaccharide-induced inflammatory response may explain the anti-inflammatory mechanism of clove extract. Lipopolysaccharide is a pro-inflammatory mitogen produced by bacterial pathogens during infection. The presence of polyphenolics in clove extract may prevent lipopolysaccharide-stimulated macrophages from expressing COX-2 [68]. Moreover, a study has reported that a high molecular weight of clove extract fraction inhibited macrophages from generating interleukin (IL)-1β, IL-6, and IL-8, which are lipopolysaccharide-induced inflammatory cytokines [69].

Conclusion

This study highlighted the potential of clove hydroethanolic extract as an antibacterial agent against *K. pneumoniae* isolated from urine samples of with UTIs. The study findings indicated the potency 500 mg/kg/day clove extract orally twice daily and 750 mg/kg/day clove extract orally once daily, which demonstrated significant antibacterial activity in female rats with UTI caused by *K. pneumoniae*. Earlier studies have also reported encouraging results in reducing bacterial resistance when combining clove extract with existing antibiotics. Therefore, future studies are recommended to explore the potential use of clove extract to create new antibiotics due to the reduced drug interaction and safety of photochemical extract.

Conflict of interests

The authors declare no conflict of interest.

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