



Review

Camel urine as a potential source of bioactive molecules showing their efficacy against pathogens: A systematic review

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ABSTRACT

Camels are highly suited for severe desert conditions and able to provide most of the natural products like urine, which has been used as alternative medicine to treat diverse infections and disorders. There is, however, a shortage and paucity of scientific reviews highlighting the antifungal, antibacterial and antiviral effects of camel urine. By better understanding its antimicrobial characteristics, our overarching aim is to provide an exhaustive overview of this valuable natural product by synthesizing and summarizing data on the efficacy of this biofluid and also describing the potential substances exhibiting antimicrobial properties. We searched three databases in order to point out relevant articles (Web of Science, Scopus and Google Scholar) until December 2022. Research articles of interest evaluating the antimicrobial effects of camel urine were selected. Overall, camel urine furnished promising antibacterial activities against gram-positive bacteria, namely *Staphylococcus aureus* (30 mm), *Bacillus cereus* (22 mm), *Bacillus subtilis* (25 mm) and *Micrococcus luteus* (21 mm), as well as gram-negative bacteria, especially *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, and *Salmonella* spp., without forgetting its efficiency on *Mycobacterium tuberculosis* as well. The excretion also showed its potency against H1N1 virus, vesicular stomatitis virus and middle east respiratory syndrome coronavirus. Similarly, the camel urine featured strong antifungal activity against *Candida albicans*, *Aspergillus niger*, *Aspergillus flavus* and dermatophytes with a minimal inhibitory concentration of 0.625 µg/ml against *Trichophyton violaceum*, 2.5 µg/ml against *Microsporum canis* and 1.25 µg/ml against *Trichophyton rubrum* and *Trichophyton mentagrophytes*. This comprehensive review will be valuable for researchers interested in investigating the potential of camel urine in the development of novel broad-spectrum key molecules targeting a wide range of drug-resistant pathogenic microorganisms.

1. Introduction

Even in droughts, extreme temperatures and harsh conditions in arid regions, Arabian camels (*Camelus dromedarius*) are considered to be one of the most powerful animals on earth because they are resilient to desert environments and able to survive and reproduce under these unfavourable climates without the adjustments required for other classes of livestock like sheep, goats, or cows (Abdalla et al., 1988). The feed of camels can depend solely on pastures for 8–10 h/day and more than 12 h/day in poor pasture. Thanks to their tough mouths, they browse preferably on high trees as well as sharp, thorny, tiny, salty and moist plants, which contain minerals and are of high nutritive value. They continue to graze even if they are thirsty and also in the presence of dehydrated shrubs, which are not palatable to other domestic mammals

(Abdalla et al., 2018). This amazing creature is still indispensable and plays a multipurpose role by supplying desert dwellers with food, transportation and trading, as well as miraculous biofluids like milk and urine that have been traditionally used as remedies for a wide range of human ailments (Abdel Gader and Alhaider, 2016).

Camel urine (CU) was mixed with milk for the treatment of enteric disorders (O'hag, Mohamedani, 2000). It was also found to be efficacious against ringworm, abscesses, and burns (Bass and Williams, 1988). Since ancient times, urine therapy was, and still is, used by nomadic people for the preservation of good health and in the cure of tuberculosis, anaemia, leprosy, colic and abdominal tumours (Al-Abdalall, 2010). It helps in reinforcing heart muscles, bone growth among children and with cleaning wounds and sores thrown into the bargain. For the sake of treating baldness, dandruff and hair loss, women in the

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Arabian Peninsula used CU as a shampoo to wash their hair in order to make it longer, lighter and more shining (Abdalla et al., 2018).

Among these numerous activities, CU remains efficacious against microbes as well (Ali et al., 2019). The investigation of Al-Zahrani and Al-Harbi (2011) on CU has shown its potent metabolites for inhibiting the growth of *Staphylococcus aureus* (*S. aureus*), including resistant strains to methicillin with the *mecA* gene. It is thus not surprising that CU was able to prevent the production of mycotoxins and to kill fungi, in particular *Aspergillus flavus* (*A. flavus*), *Candida albicans* (*C. albicans*) and *Fusarium oxysporum* (*F. oxysporum*), which infect humans (Gole, 2020). There has been an increasing interest in discovering alternative methods of treating infectious diseases. Nonetheless, available scientific backups are scant and meagre. Hence, this paper has managed to systematically appraise the relevant surveys scrutinizing the effect of CU on bacteria, fungi and viruses. The aim of the present investigation is to summarize and characterize the antimicrobial effects of this bioactive fluid.

2. Methods

2.1. Literature review

A systematic search of literature was carried out following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). It was based on studies focusing on the antimicrobial effects of CU. Listed below are the databases that were employed for this exhaustive search: Scopus, Google Scholar and Web of Science from 1986 until December 2022. The following keywords were used: “Antibacterial” OR “Antimicrobial” OR “Antifungal” OR “Antiviral” AND “Urine” AND “Activity” OR “Effect” AND “Camel” OR “Dromedary” OR “Dromedarius”.

2.2. Study inclusion and exclusion criteria

Only research articles originally written and published in English that were reporting the effect of CU on all types of microorganisms were included. Duplicate articles, those which were lacking the full text or were off-topic, review articles, conference proceedings, editorial letters, book chapters, case reports and bibliographies were excluded from this review.

2.3. Extraction and management of dataset

All the articles were read by two independent reviewers. In case of any discrepancy, a consensus was reached through discussion. The remaining articles that met the inclusion criteria contained all the information about the antimicrobial activity of camel urine. The data extraction form corresponded to (1) storage and quantity of camel urine, (2) camel characteristics, (3) geographical locations where urine samples were isolated, (4) types of microorganisms used in the survey, (5) methodology and (6) interpretation with conclusion. All these data were tabulated in Table 1.

3. Results

3.1. Overview of the included studies

As a result of the literature research, 130 837 articles were found in three databases, including 7 articles from Scopus, 126 000 articles from Web of Science and 4830 articles from Google Scholar. Afterwards, 1800 articles were removed due to duplication and 128 997 articles were removed through the process of evaluating their titles and summaries. After reading documents in their entirety by applying exclusion and inclusion criteria, 18 articles were removed from the 37 remaining articles, including fourteen non-relevant articles and four review articles. In total, this paper included 19 articles that fulfilled all the required criteria. The flow-diagram shown in Fig. 1 presents the process for

selecting and excluding studies.

3.2. Study characteristics

In total, 129 037 articles were found in 3 databases after removing duplicates, as mentioned in Fig. 1. In line with the established inclusion criteria, nineteen selected articles met the qualifications for the ongoing systematic review. Regarding these essays, nine reported the effect of CU on bacteria (Mostafa and Dwedat, 2016, Bakhsh et al., 2019, Humaid, 2016, Bayed et al., 2020, Elbehiry et al., 2021, Shinashal, 2014, A-Ameri et al., 2015, Abdullahi et al., 2021, Sumia et al., 2016), four mentioned its activity on fungal isolates Al-Abdalall, 2010, Al-Awadi and Aljudaibi, 2014), and two registered the antiviral characteristics of CU (Noor et al., 2015, Al Attas, 2019), while four studies investigated the product on both bacterial and fungal species (Al-Bashan, 2011, Khedr, 2016, El-Desoukey, 2020, El-Shahawy et al., 2010).

Two studies used urine from virgin female camels (Bayed et al., 2020, Osman et al., 2016), one used breeding female camels and nine studies investigated both female and male CU, whereas five studies didn't mention the gender of the camels from which the urine was taken. Additionally, four studies assessed the effect of the prophet medicine fraction (PMF) which is the bioactive fraction extracted from dried CU (Bakhsh et al., 2019, El-Shahawy et al., 2010, Noor et al., 2015, Al Attas, 2019). As for the geographic origin of published studies, six were published in Saudi Arabia, four were conducted in Sudan, three came from Egypt, two from Yemen, one took place in Iraq, another in Ethiopia and two studies were carried out with international collaboration – between Saudi Arabia and Germany and between Saudi Arabia and Egypt. Fig. 2 displays the global distribution of included papers in the antimicrobial activity of CU by country.

3.3. Camel urine against gram-positive bacteria

In our systematic review, nine studies from our sample highlighted the significant effects of CU on gram-positive bacteria, especially *Streptococcus pyogenes* (*S. pyogenes*), *Streptococcus agalactiae* (*S. agalactiae*), *S. aureus*, *Bacillus cereus* (*B. cereus*), *Bacillus subtilis* (*B. subtilis*), coagulase-negative *Staphylococci*, *Enterococcus* spp. and *Micrococcus luteus* (*M. luteus*).

In vitro, Sumia et al. (2016) revealed that concentrated CU was more effective against *S. aureus*, with a 30 mm diameter inhibition zone observed after 24 h of incubation at 37 °C. In contrast, the inhibitory zones were 12 mm and 13 mm for fresh and neutralized urine, respectively. Similarly, another study demonstrated the presence of clear inhibition zones of virgin female CU against *S. aureus* isolated from wound infections by the use of both 50 % and 100 % titres (Bayed et al., 2020). These results are consistent with those of Abdullahi et al. (2021) that showed the importance of CU in inhibiting *S. aureus* susceptible to gentamycin (10.66 mm) by the use of the disc diffusion method; its minimum inhibitory concentration (MIC) was 10.60 %. They also showed that there is no difference between male and female CU. *In vivo*, (Shinashal, 2014) confirmed the efficacy of CU on a rabbit's burned skin infected by *S. aureus*, as can be seen by its healing after 48 h compared with rabbits treated by dicloxacillin, in which the healing lasted more than 72 h, or the control group, which had complete healing within 120 h. Also, they identified that CU was able to inhibit the growth of bacteria tested on their appropriate media.

A recent study by El-Desoukey (2020) reported that the diameters of inhibition zones by the well diffusion method were 23 mm and 11 mm with CU alone for *S. aureus* and *Bacillus* spp., respectively, and they were enhanced by adding camel milk to become 24 mm and 12 mm. By the same means, Humaid (2016) indicated reduced diameters (5 mm and 4 mm) for both bacteria. Nevertheless, by heating, sterilizing CU and extending the incubation period to 72 h, they measured 12 mm and 22 mm for *S. aureus* and *B. cereus*, respectively. Also, the treated CU was effective against *M. luteus* (21 mm). Likewise, another study by Khedr

Table 1
Data extraction table.

Country	Sample quantity and storage	Camel characteristics	Type of Microorganism used in the survey	Methodology	Interpretation with conclusion	References
Saudi Arabia & Egypt	Not mentioned	Not Mentioned	<p>*<i>Salmonella typhi</i> and <i>Escherichia coli</i> (<i>E. coli</i>)</p> <p>*Fungal species were <i>Trichophyton rubrum</i> (<i>T. rubrum</i>), <i>Epidermophyton floccosum</i> (<i>E. floccosum</i>), <i>Aspergillus fumigatus</i>, <i>Microsporium canis</i> (<i>M. canis</i>)</p> <p>*<i>Staphylococcus citreus</i>, <i>Bacillus subtilis</i> (<i>B. subtilis</i>)</p>	<p>*A lyophilized form of camel urine (CU) after its extraction using the following solvents: CHCl₃, ethyl acetate, n-butanol or methyl alcohol.</p> <p>*The paper disc diffusion assay was employed to test the antimicrobial properties of PMF (bioactive fraction extracted from dried CU) and the crude PM 701 (dried CU).</p> <p>*The agar dilution method was used to determine the minimal inhibitory concentration (MIC).</p> <p>*The agar plate technique was used to test the antifungal effects of PMF and PM701.</p> <p>Effect of CU on aflatoxins: The agar diffusion method was used in this testing.</p> <p>Effect of CU on fungal mycelium growth: Dry weight of fungi and linear growth of fungal mycelia</p>	<p>The antibacterial and antifungal activities are due to:</p> <p>*Higher contents of metal ions in PM701.</p> <p>*Heavy metals in PM 701 sample inhibited the generation of <i>Aspergillus</i> conidial spores.</p> <p>CONCLUSION: The crude extract PM701 of CU was more efficient against bacteria and fungi than the pure extract PMF.</p>	(El-Shahawy et al., 2010)
Saudi Arabia	Urine specimens were kept at 4 °C for a maximum of 7 days.	Female camel (<i>Camelus Dromedarius</i>)	<p>Fungi isolates from pulse seeds such as <i>Aspergillus niger</i> (<i>A. niger</i>) <i>Aschocayta</i> sp., <i>Sclerotinia sclerotiorum</i>, <i>Aspergillus flavus</i> (<i>A. flavus</i>), <i>Pythium aphanidermatum</i>, <i>Rhizoctonia solani</i> and <i>Fusarium moliniform</i>.</p>	<p>Effect of CU on aflatoxins: The agar diffusion method was used in this testing.</p> <p>Effect of CU on fungal mycelium growth: Dry weight of fungi and linear growth of fungal mycelia</p>	<p>*Plasmolysis was generated by urine's salts.</p> <p>*Continued exposure of bacterial cells to CU led to their non-disintegration (bacteriolysis) with an appearance of bacterial chromosome without plasmids.</p> <p>CONCLUSION: The remarkable activity of CU on fungi was only noticed at high doses.</p>	(Al-Abdalall, 2010)
Saudi Arabia	12 urine samples	Healthy camels of one breed with both sexes whose ages fall between 6 months and 4 years.	<p>*<i>Candida albicans</i> (<i>C. albicans</i>) and <i>A. niger</i></p> <p>*<i>Staphylococcus aureus</i> (<i>S. aureus</i>), <i>Streptococcus pyogenes</i> and <i>Streptococcus agalactiae</i></p> <p>*<i>E. coli</i>, <i>Klebsiella pneumoniae</i> (<i>K. pneumoniae</i>) and <i>Pseudomonas aeruginosa</i> (PA)</p>	<p>*The method used to assess the antimicrobial activity was the disc diffusion mean.</p>	<p>*CU contains bacteria (the resident microflora that colonize the urethra) and bacteriophages.</p> <p>*Biochemical components of CU increase in hydrated conditions than dehydrated ones. This raise emanates from bushes and wild plants in the desert.</p> <p>* Potassium is the dominant ion excreted, but when the camel consumes certain types of salty plants, sodium can become the dominant ion.</p> <p>CONCLUSION: CU has a distinctive ability to kill bacteria and fungi. This effect is due to bacteriophages, biochemical components and salty wild forage that camels feed on. This activity is related to:</p>	(Al-Bashan, 2011)
Iraq	24 samples of urine	Camels of one breed and of both sexes whose ages fall between 8 months to 3 years	<p>*<i>E. coli</i> strains were isolated from science's college.</p> <p>*<i>S. aureus</i> strains were obtained from burn patients through the collection of swab specimens.</p>	<p>For systemic infection: *12 rabbits aged between 6 and 10 months were infected orally by <i>E. coli</i>. They were also divided into 3 groups (4 rabbits / group).</p> <p>*The 1st group was treated by urine, the 2nd by gentamicin and the 3rd by saline solution.</p> <p>For cutaneous infection: *The thigh of 12 rabbits used in this survey were burned then infected with <i>S. aureus</i>.</p> <p>* The 12 infected rabbits were separated into three groups. The 1st one was treated by urine, the 2nd by dicloxacillin and the 3rd by saline solution.</p>	<p>*The compounds of CU like water, urea, hormones and metabolites, including corticosteroids, and factors that aid in recovery like urea, antibiotics and salts.</p> <p>*The immunity which is manifested by antibodies was able to kill fungi, viruses and bacteria.</p> <p>CONCLUSION: In comparison with gentamicin, this investigation showed <i>in vivo</i> that CU is an active medicine in the cure of diarrhea after 20 h of its use.</p>	(Shinashal, 2014)

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Table 1 (continued)

Country	Sample quantity and storage	Camel characteristics	Type of Microorganism used in the survey	Methodology	Interpretation with conclusion	References
Egypt	CU was collected in bottles, which were immediately transported to the laboratory.	Healthy camels lived in the desert	Three fungi were tested in this survey: * <i>A. niger</i> and <i>Fusarium oxysporum</i> (<i>F. oxysporum</i>) isolated from plants. * <i>C. albicans</i> isolated from clinical specimens.	*The filter paper discs were saturated with 100 µl of CU. *The incubation period lasted 7 days for <i>A. niger</i> and <i>F. oxysporum</i> at 28 °C while <i>C. albicans</i> required only 48 h at 30 °C. *All tests were performed in triplicate.	*This antifungal activity is due to the high alkalinity of CU as a result of high concentrations of K, Mg, Ca and proteins, and low concentrations of carbohydrates and cellulose. *The antimicrobial effect was intensified by active elements that camels extracted from desert pastures during their feeding. *CU contains bacteria that are able to survive in harsh conditions such as high osmotic concentrations, alkalinity and lack of nutrition. CONCLUSION: CU is an effective and durable treatment for both human and plant fungal infections and does not appear to have negative side effects. It was showed that the fungicidal properties of CU remained stable even after heating or storage.	(Al-Awadi and Aljudaibi, 2014)
Saudi Arabia & Egypt	150 mg/g of PMF from the powdered PM 701 of CU.	Not mentioned	*Vero cells in a tissue culture flask that have been pre- cultivated were inoculated with sterile vesicular stomatitis virus (VSV) (which are a type of cell line that originated from the kidney tissue of an African green monkey). *Human hepatocellular carcinoma cells HpeG2 cell line (ATCC- HB-8065) were used to assess the cytotoxicity of PMF.	*PMF concentrations were prepared in Eagle's Minimum Essential Medium (EMEM) to obtain 60, 30, 15 µg/ml. *Tissue culture plates of 96 wells were cultured by 10 ⁵ Vero cells/ml. *100 µl of PMF were added to each well of the plates without forgetting to use untreated plate as control. *VSV was diluted ten times in EMEM, all the dilutions were added to the plates in which the incubation was carried out at 37 °C per 24 h before and after the addition of VSV.	*The antiviral activity is due to the lysozyme enzyme present in CU. *CU may disrupt the structure of viral epitopes, preventing the virus from binding to cell receptors. It was determined that the PMF's chemical structure could disrupt the integration of viral epitopes, which in turn influences the replication enzymes of the virus. CONCLUSION: The PMF has a significant impact on virus replication, and further research should be conducted using DNA and RNA viruses as well as those that cause cancer to optimize its potential as a fast-acting antiviral agent.	(Noor et al., 2015)
Yemen	Not mentioned	Mature male, mature female and virgin female camels	50 PA and 150 other bacteria were isolated from different specimens (ear, burn and wound swabs) in patients.	Mueller Hinton agar plates were previously inoculated by PA isolates, then discs soaked by fresh CU were placed down.	This phenomenon is interpreted by the bacteria present as well as bacteriophages (that are characterized by a bactericidal effect) found naturally in CU. CONCLUSION: It is suggested that CU should be manufactured and used as treatment for multidrug-resistant PA.	(A-Ameri et al., 2015)
Egypt	4 °C / no more than 7 days prior to being utilized in the research.	Not mentioned	<u>55 clinical isolates:</u> *10 methicillin-resistant <i>Staphylococcus aureus</i> (MRSA). *10 extended-spectrum beta-lactamases (ESBL) producing gram-negative bacilli (4 <i>Klebsiella</i> spp., 4 <i>E. coli</i> , 1 <i>Acinetobacter baumannii</i> , 1 <i>Enterobacter</i> spp.). *10 carbapenemase-producing Gram-negative bacilli: 6 <i>K. pneumoniae</i> , 2 PA, 1 <i>Proteus mirabilis</i> (<i>P. mirabilis</i>) and 1 <i>Citrobacter</i> spp). *10 multi-drug resistant coagulase negative <i>Staphylococci</i> (CoNS). *10 multi-drug resistant <i>Enterococcus</i> spp.	Media containing diverse CU concentrations (100 %, 75 %, 50 % and 25 %) were inoculated by 10 µl of diluted bacterial isolates.	*The antimicrobial activity become more potent after storage of CU and heating to 100 °C. *This activity is an outcome of extended titres of proteins, magnesium, calcium and potassium as well as minimal traces of cellulose and carbohydrates. *CU was able to stimulate an immune response and does not possess a toxic effect on peripheral blood mononuclear cells. CONCLUSION: This study clearly demonstrates that CU has the ability to fight against bacteria, including those that are resistant to antibiotic drugs.	(Mostafa and Dwedar, 2016)

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Table 1 (continued)

Country	Sample quantity and storage	Camel characteristics	Type of Microorganism used in the survey	Methodology	Interpretation with conclusion	References
Sudan	Urine samples were collected aseptically then stored at 4 °C.	Virgin female camel	<i>Alternaria alternata</i> (A. <i>alternata</i>) is a fungus which caused early blight, which is among the highest prevalent diseases affecting tomatoes.	Antifungal activity was determined by inoculating fungal discs in PDA media mixed with CU at different concentrations (+control). Media were kept at 27 ± 2 °C for 10 days.	CONCLUSION: By the evaluation of CU on A. <i>alternata</i> in laboratory essays, it was probed to have a promising therapeutic effect.	(Osman et al., 2016)
Sudan	200 ml of urine were poured in bottles and freeze-dried by a freeze-dryer machine.	Female and male camels	*All these fungi were clinical isolates obtained from hair, skin, and nail specimens. *A total of 85 dermatophytes strains: <i>Trichophyton mentagrophytes</i> (n = 11), <i>T. rubrum</i> (n = 33), <i>Trichophyton violaceum</i> (n = 15), <i>E. floccosum</i> (n = 7), <i>M. canis</i> (n = 10), <i>Microsporium gypseum</i> (n = 5), and <i>Trichophyton tonsurans</i> (n = 4) were investigated.	Inoculum suspensions: *Tested dermatophytes were inoculated for 7 days at 28 °C on PDA media. *5 ml of sterile distilled water was added on each colony then filtrated with pore diameter of 8 mm. *The resulted inoculum contains only spores. Procedure: Polystyrene microtitre plates with 96 wells were all inoculated by CU at different titres and dilutions of fluconazole and ketoconazole drugs too. Each plate was filled with 100 ml of the diluted inoculum. *Each well was filled with 10 µl of resazurin indicator solution and kept for 2 days at 37 °C. *By well diffusion assay, the antibacterial effect of CU was discovered.	CONCLUSION: CU was found to be a highly effective antifungal agent against dermatophytes, surpassing the performance of the synthetic drug fluconazole and in comparison, to that of ketoconazole. It could potentially be a viable alternative to other drugs used in the treatment of dermatomycosis.	(Kabbashi and Al Fadhil, 2016)
Yemen	*2 weeks of storage at 4 °C *Three types of urine were adopted: raw, heated and sterilized.	Camels of both sexes whose ages fall between 6 months and 4 years	*Six clinical bacteria: <i>S. aureus</i> , <i>Salmonella</i> spp, <i>Micrococcus lotus</i> , <i>E. coli</i> , <i>Bacillus cereus</i> and PA.	*By well diffusion assay, the antibacterial effect of CU was discovered.	*This phenomenon might be due to the bacteriophages found naturally in CU. *CU was characterized by a high immune system, which was manifested by antibodies to combat fungi, bacteria and viruses. * The immunity was related to the presence of urea and salts. CONCLUSION: CU could be employed as alternative medicine for the cure of bacterial ailments.	(Humaid, 2016)
Saudi Arabia	Urine specimens were kept at –80 °C in separate containers.	Adult camels (1–5 years old)	*Fungi: A. <i>flavus</i> (ATCC 204304) *Gram-negative strains: PA (ATCC 10145), <i>E. coli</i> (ATCC 11775). *Yeasts: <i>C. albicans</i> (ATCC26555) *Gram-positive strains: <i>B. subtilis</i> (ATCC 6051) <i>S. aureus</i> (ATCC 12600).	*The antimicrobial effect was tested by the disc diffusion method. They used three types of samples as follows: fresh CU, enzymatic hydrolysed CU and a standard solution was prepared with the same titres of bioactive compounds that are commonly present in CU. *Negative control: dimethyl sulfoxide (DMSO). *Positive control: ampicillin and amphotericin B.	It was reported that these activities are attributed to high concentrations of biologically active materials that CU contains like cinnamic acid, azelaic acid, phenol, salicylic acid and p-cresol. CONCLUSION: Adult CU and a prepared standard mixture (which encompassed the major acidic and phenolic elements isolated after the use of gas chromatography-mass spectrometry) were effective against bacteria and fungi after 72 h of incubation.	(Khedr, 2016)
Sudan	* 60 samples (5 ml) of urine. *Three types of urine (Normal, Neutralized and concentrated)	Camels of both sexes (<i>Camelus dromedarius</i>) whose ages fall between 4 months and 4 years old.	*The bacterial isolates were as follows: PA, <i>S. aureus</i> , <i>Enterobacter cloacae</i> and <i>E. coli</i> , <i>Salmonella</i> spp	*In this study, the disc diffusion method (6 mm) and agar diffusion method (wells of 8 mm diameter) were used.	*The presence of antimicrobial elements in shrubs and desert pastures were possibly responsible for this antibacterial effect. *CU may raise the permeability of the cell wall to antibiotic. CONCLUSION: Concentrated CU has a potent ability to inhibit bacterial growth. Additionally, agar well diffusion was recorded as a better method than disc diffusion mean.	(Sumia et al., 2016)

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Table 1 (continued)

Country	Sample quantity and storage	Camel characteristics	Type of Microorganism used in the survey	Methodology	Interpretation with conclusion	References
Saudi Arabia	From dried CU (PM701), a yellowish powder was obtained which is an active biological fraction named PMF (Prophet Medicine fraction).	Not mentioned	*10 samples of sputum which were in good conditions, were collected from the hospital. * <i>Mycobacterium tuberculosis</i> (MTB) was isolated by using BACTEC-960 system which is an automated system created for rapid detection of mycobacteria.	*The different concentrations (5 %, 7.5 %, 10 %, 12.5 % and 15 %) of PMF extraction were prepared by solving the dried CU (PM701) in methyl alcohol. *Various rates of PMF as well as commercial drugs were all assessed on MTB in BACTEC system 960.	CONCLUSION: This paper indicated that MTB is not influenced by PMF at a titre range of either 5 % or 15 %, however, 10 % concentration of PMF is more efficacious in comparison with Rifampicin.	(Bakhsh et al., 2019)
Saudi Arabia & Germany	PMF was isolated from dried camel urine and was stored at 2–8 °C.	Not mentioned	*Influenza A, virus subtype H1N1 and Transmissible gastroenteritis Virus (TGEV) which is used as a model virus for Middle East respiratory syndrome coronavirus (MERS-CoV). *MERS-CoV virus targeted the ST75/2 cells (fetal testis cells of swine). *H1N1 virus targeted the MDCK/63 (Madin-Darby canine kidney cell lines used as epithelial cell models).	*After warming up to 37 °C, 2.95 ml of aqua bidest (double distilled water) was added to 0.75 g of PMF. *Virus suspensions were prepared in cell culture flasks of 25 cm ² (each virus with its targeted cell). Accordingly, the supernatant was obtained after centrifugation and the induction of the cytopathic effect.	* Zinc has been shown to prevent the amplification of TGEV within cells by blocking protein production. However, it has not a cytotoxic effect. * Copper ions also decrease the ability of phages to cause infections. * The current study suggested that both copper and zinc displayed a crucial role in antiviral and virostatic effects of PMF. CONCLUSION: The study found that treatment with PMF induce a remarkable decrease in the levels of virus replication and the cellular one too. It was also suggested that PMF may have antiviral properties.	(Al Attas, 2019)
Sudan	*60 samples of CU. *Three urine specimens were used in this study: raw, concentrated and neutralized by HCl (10 %).	Virgin camels consuming desert pasture aged 5 years	<i>K. pneumoniae</i> , <i>S. aureus</i> , <i>E. coli</i> , <i>P. mirabilis</i> were obtained from individuals suffering from infected wounds.	Mueller Hinton agar plates were prepared by different concentrations (100 %, 50 %, 25 % and 12.5 %) of CU.	The antibacterial effect of CU was not explained. CONCLUSION: The inhibitory titre of CU against tested bacteria is 50 %.	(Bayed et al., 2020)
Egypt	CU was kept in the fridge till used.	Not mentioned	Pathogenic strains collected from animals used in this study were as follows: <i>C. albicans</i> , <i>E. coli</i> , <i>Bacillus</i> spp, PA, and <i>S. aureus</i> .	To evaluate the antimicrobial activity of CU, an agar well diffusion assay was employed.	*The antimicrobial activity of CU may be explained by the consumption of halophyte segments and desert pastures. CONCLUSION: CU possessed antimicrobial impacts against pathogens like <i>E. coli</i> , <i>S. aureus</i> , <i>Bacillus</i> spp., PA and <i>C. albicans</i> .	(El-Desoukey, 2020)
Ethiopia	13 samples of CU	*6 male camels 7 female camels (Virgin-lactating and pregnant). *Of the 7 female camels: 1: lactating Camel 1: pregnant Camel 2: virgin Camel 3 camels whose the status did not mentioned in the survey.	*Clinical isolates of bacterial pathogens were: <i>Citrobacter</i> spp, <i>E. coli</i> , <i>K. pneumoniae</i> and <i>S. aureus</i> .	The antibacterial activity and the MIC were assessed by the disc diffusion method; discs of 6 mm were impregnated by each titre of CU (100 %, 50 %, 25 %, 12.5 %, 6.25 %) then filled on Mueller Hinton agar.	CONCLUSION: The results showed the potential antibacterial effect of CU against tested bacterial strains in order to fight infectious diseases.	(Abdullahi et al., 2021)
Saudi Arabia	300 ml /coolers with cold accumulators until use.	Virgin and breeding female camels (2–10 years)	*20 <i>E. coli</i> identified from mastitic cow's milk. *10 clinical <i>E. coli</i> from the Hospital	The antibacterial effect of sterilized CU with 4 different concentrations (100 %, 75 %, 50 % and 25 %) was determined using the disc diffusion method.	* The active compounds of urine were extended by heating. *The high alkalinity of CU may be attributed to its high levels of proteins, Ca, Mg and K and reduced levels of carbohydrates and cellulose. *Numerous types of vegetation with high salt concentrations CONCLUSION: CU was efficacious even on multi-drug resistant tested <i>E. coli</i> .	(Elbehiry et al., 2021)

(2016) found that fresh CU possessed less antibacterial effects (12 mm and 9 mm) than hydrolysed CU (17 mm and 15 mm) for *S. aureus* and *B. subtilis*, respectively. After treating *B. subtilis* with PM-701 (a bioactive fraction obtained from dried CU), the diameter of the inhibition zone increased to 25 mm. The same author measured 21 mm for *Staphylococcus citreus* (El-Shahawy et al., 2010).

Indeed, the disks soaked with CU showed a remarkable inhibition zone against *S. pyogenes*, *S. agalactiae* and *S. aureus*. Overall, Mostafa and Dwedat (2016) revealed the efficiency of CU against even methicillin-resistant *Staphylococcus aureus* (MRSA), *Enterococcus* spp., and multi-drug resistant coagulase-negative *staphylococci*.

3.4. Camel urine against gram-negative bacteria

Within the family *Enterobacteriaceae*, *Escherichia coli* (*E. coli*) is the most-studied microorganism; it is known to cause urinary tract infections, many diarrheal diseases and neonatal meningitis (Kaper et al., 2004). All the included studies appear to emphasize the significant effect of CU on this frequently deadly pathogen. Sumia et al. (2016) indicated the presence of inhibition zones on Mueller Hinton agar media by measuring 14 mm, 15 mm and 30 mm diameters for fresh, neutralized and concentrated CU respectively. They also mentioned that the antimicrobial activity of male CU was more effective than the female CU. Bayed et al. (2020) confirmed the efficiency of camel excretion by the use of both 50 % and 100 % concentrations. Notably, the study done by Humaid (2016) pointed out that *E. coli* had the largest inhibition zone of all tested bacteria in his trial. These zones were identified by diameters of 12 mm, 16 mm and 23 mm whilst prolonging the incubation period to 72 h. Moreover, a determination of the antibacterial activity of CU was undertaken according to the disc diffusion method by Abdullahi et al. (2021), who measured 14.73 mm as the diameter of inhibition zone. Interestingly, another study put the spotlight on systemic infections of rabbits by *E. coli*. The treatment of infected rabbits with CU intravenously showed their recovery after only 15 h in comparison with treatment by gentamicin (24 h) or by saline (96 h). For *in vitro* experimental studies, the discs soaked with CU and applied to the surface of the seeded plates presented an inhibition zone (18 mm) larger than those impregnated by gentamicin (12 mm) (Shinashal, 2014). On the same microorganism, a study by Khedr (2016) explicitly captured the significant role of hydrolysed CU, whereby the diameter became wider (20 mm) than the one for raw CU (11 mm). By using the well diffusion method, (El-Desoukey (2020) registered a diameter of 21 mm induced by CU in inoculated media. Additionally, another study focusing on the effect of dried CU (PM701) revealed its ability to inhibit the growth of *E. coli*; this inhibition zone was conferred by a diameter of 20 mm (El-Shahawy et al., 2010). On the whole, Mostafa and Dwedat (2016) concluded that CU was also efficient on extended-spectrum beta-lactamases (ESBLs) and carbapenemase-producing *E. coli* by the use of the following titres: 10 %, 7.5 % and 5 %. In brief, a recent study by Elbehiry et al. (2021) recorded that multidrug-resistant *E. coli* were inhibited by virgin CU (14 mm, 17 mm and 28 mm) with the use of titres of 50 %, 75 % and 100 % respectively. Notwithstanding, the breeding CU was less effective than the previous one; measuring only 18 mm with the 100 % titre. However, with other tested concentrations, a bacterial growth around the discs was noticed.

Klebsiella pneumoniae (*K. pneumoniae*) was identified as the leading cause of hospital-acquired and opportunistic infections, mainly in patients having an impaired immune system (Clegg and Murphy, 2016). Even with antibiotic therapy, the multidrug-resistant strains of this lactose fermenting bacteria were characterized by a high fatality rate, reaching 47.66 % (Xu et al., 2017). In the present review, four studies stated the remarkable effect of CU on this pathogen; the study by Abdullahi et al. (2021) used the disc diffusion assay which exhibited the largest diameter (18.63 mm) among all screened bacteria. Closely following, Al-Bashan (2011) and Bayed et al. (2020) verified the notable antibacterial activity of CU at concentrations of both 50 % and 100 %.

Although, on ESBL- and carbapenemase-producing *K. pneumoniae*, it was evinced that CU was able to inhibit their growth on their suitable media (Mostafa and Dwedat, 2016).

Acute diarrheal diseases, typhoid fever and foodborne infections were the most common manifestations of *Salmonella*. These stringent illnesses were associated with an elevated rate of morbidity and mortality, with around 200 000 deaths related to typhoid each year (Als et al., 2018). Our potent metabolic excretion of interest was effective against this pathogen too; passing by fresh, neutralized and concentrated CU, Sumia et al. (2016) measured different diameters of inhibition zones – 14 mm, 17 mm and 31 mm, respectively. In addition, the study by Humaid (2016) corroborated that the sterilized CU has more antibacterial activity (17 mm) than the heated CU (11 mm), while the fresh CU presented only a smaller inhibition zone (5 mm). The same finding was obtained by El-Shahawy et al. (2010), who employed PM-701 extracted from CU, which proved to have an inhibition zone in which the diameter was 18 mm.

Continuing in the family of *Enterobacteriaceae*, *Enterobacter cloacae* was responsible for causing pneumonia, skin, tissue and nosocomial infections among inpatients in the intensive care unit (ICU), with a death rate reaching 30 % (Ioannou et al., 2022). First, the study by Sumia et al. (2016) was the only study reporting the largest diameter (32 mm) on Miller Hinton agar using concentrated CU. Secondly, an assessment of the antibacterial effect of CU against multi-drug resistant *Enterobacter* spp. was also realized by Mostafa and Dwedat (2016), who recorded the absence of growth on inoculated plates at the following titres: 5 %, 7.5 % and 10 %.

The genus *Citrobacter* was associated with meningitis, gastroenteritis as well as nosocomial outbreaks, mostly among neonates and immunocompromised individuals (Yuan et al., 2019). Actually, the findings of Abdullahi et al. (2021) highlighted that the best effect of CU was shown by the virgin camels (21.83 mm), followed by breeding CU (15 mm) then the one from lactating camel (10 mm). Besides, the usage of CU even on multi-drug resistant *Citrobacter* spp. indicated a high ability to inhibit its growth (Mostafa and Dwedat, 2016).

Belonging to lactose fermenting bacteria, *Proteus mirabilis* (*P. mirabilis*) was most noted for causing complicated urinary tract infections (UTI), distinctly among patients with long-term indwelling catheters (Schaffer and Pearson, 2015). Indeed, the study conducted at Kassala University Faculty of Medicine and Health Sciences, Sudan showed that CU was more effective versus this frequent pathogen at both concentrations (50 % and 100 %) (Bayed et al., 2020). Surprisingly, CU also revealed a great inhibition zone against carbapenemase-producing *P. mirabilis*, which was well-known for increasing the mortality rate owing to uncontrolled and indiscriminate antibiotic usage (Mostafa and Dwedat, 2016).

Moving to non-fermenting bacteria, Sumia et al. (2016) stated that the highest antibacterial effect of CU (32 mm) was attributed to *Pseudomonas aeruginosa* (*P. aeruginosa*). The studies published in Saudi Arabia drew attention to the potency of CU in obstructing the growth of this pathogen, which was recognized as one of the top-listed microorganisms causing healthcare-associated infections (Behzadi et al., 2021). Those were the studies where the two authors, El-Desoukey (2020) and Khedr (2016), measured the same inhibitory zone (16 mm) by the use of hydrolysed and concentrated CU. Comparably, the results discovered by Al-Bashan (2011) and Humaid (2016) were in line with the previous studies in which they asserted the significant capacity of CU against this species. In particular, carbapenemase-producing *P. aeruginosa* was registered among a critical subset of pathogens by the World Health Organization (WHO) which require novel antibiotics extracted from alternative medicine. For instance, A-Ameri et al. (2015) and Mostafa and Dwedat (2016) reported the value of female and male CU against this multi-drug resistant bacilli, mainly after 72 h of incubation at 37 °C.

From our review, the study by Mostafa and Dwedat (2016) in Egypt was the only study reporting the virtue of CU versus ESBL producing *Acinetobacter baumannii*, which are also known as one of the sources of

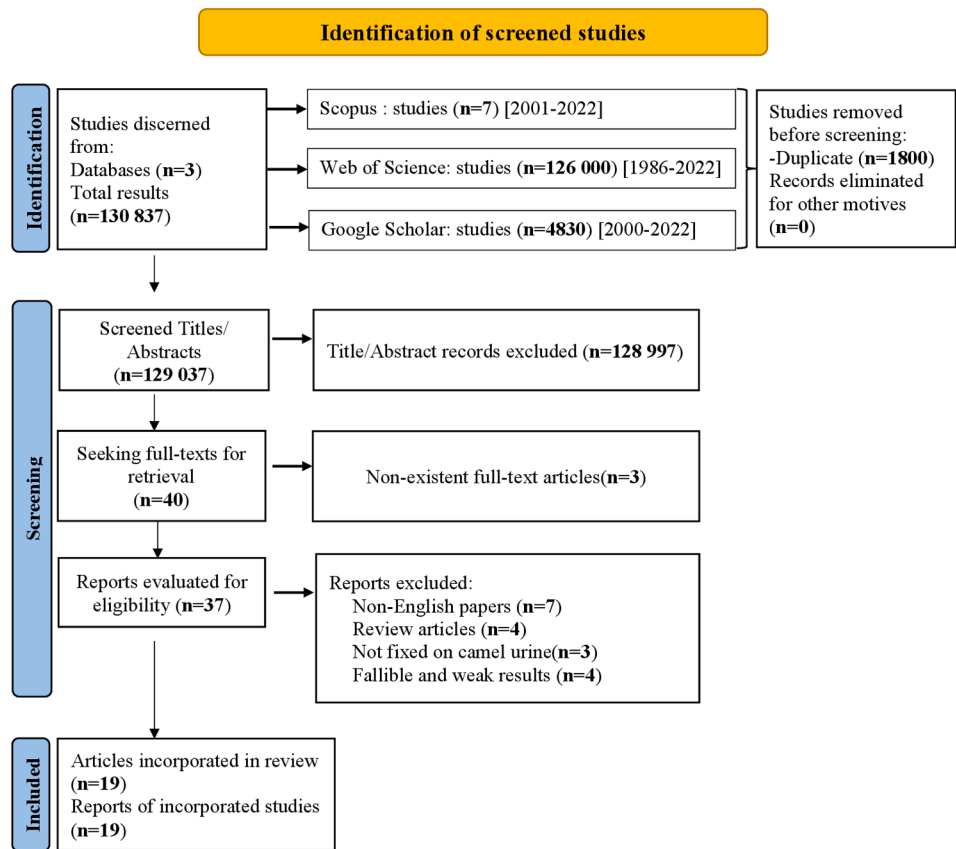


Fig. 1. Identification of included articles in this review using PRISMA guidelines (meta-analysis).

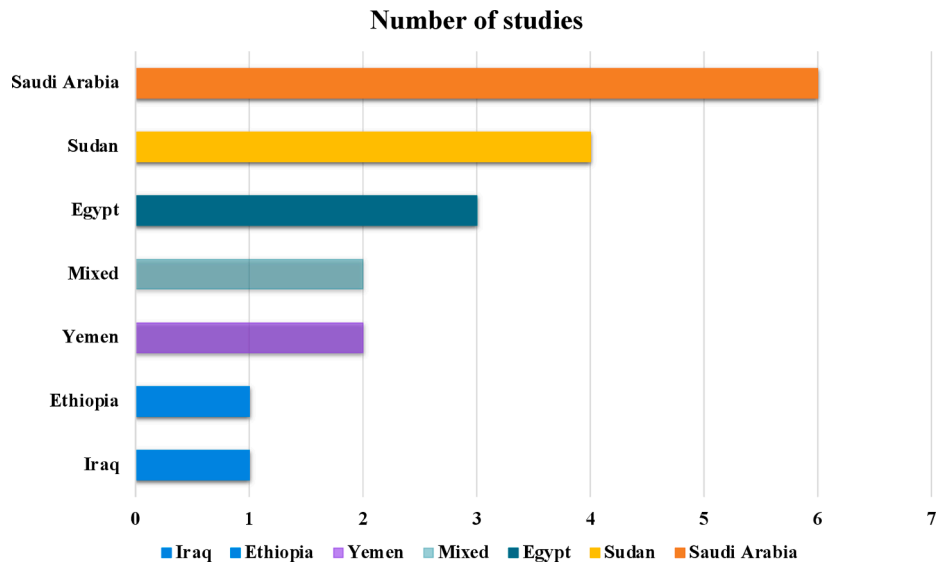


Fig. 2. Distribution and number of included studies by country of antimicrobial activity of Camel's urine. Mixed: Study conducted in multiple countries.

hospital-acquired infections, with a mortality rate ranging from 33 % to 60 % (Patel et al., 2019).

3.5. Camel urine against *Mycobacterium tuberculosis*

Despite the rapid growth of technology, the mortality of tuberculosis remains high, reaching 25 % among adults and 30 % for immunosuppressed patients. *M. tuberculosis* was the main causative pathogen of this severe disease (Pai et al., 2016). In fact, the PMF at the dose of 10 % was

the only element which was evaluated against this bacillus and showed the same potent effect by diminishing the number of bacteria on a mycobacteria growth indicator tube (MGIT), as well as with GeneXpert, in comparison to their treatment by rifampicin (Bakhsh et al., 2019).

3.6. Camel urine against viruses

Two studies that were conducted in Saudi Arabia postulated that PMF play a notable role in decreasing the growth rate of the following

RNA viruses: H1N1 virus, vesicular stomatitis virus (VSV) and middle east respiratory syndrome coronavirus (MERS-CoV). Certainly, after culturing H1N1 virus; TGEV, which was used as a model virus for MERS-CoV in MDCK/63 cells (Madin-Darby Canine Kidney cell lines) and ST75/2 cells (fetal testis cells of swine), Al Attas (2019) noted that the use of lyophilized powder of CU at a dose of 20.34 % showed a decline in MERS-CoV titre by 99.5 % after 60 min, and no residual virus could be detected after 240 min. The same author concluded that the identical PMF concentration inhibited 98.90 % of the subtype of influenza A virus H1N1 on their appropriate cells after 1 h and 99.99 % after 4 h.

On the other hand, livestock such as horses, cattle and swine could be affected by a zoonotic illness, vesicular stomatitis, which could be transmitted to humans through direct contact with contaminated wounds and saliva found in these animals. It is responsible for diverse symptoms like fever, headache, fatigue and myalgia. This disease influenced international trade and inflicted high economic costs to producers (Pelzel-McCluskey et al., 2021). This is why Noor et al. (2015) had specifically identified the capacity of the fraction extracted from CU against VSV virus (previously cultured in Vero cells) by a decrease in its infectivity titer after 15 min, then by the absence of the virus after 75 min.

3.7. Camel urine against fungi

Al-Bashan (2011) investigated the antifungal effect of CU versus *C. albicans*, which is a commensal and natural member of the microbiota of mucosal surfaces and the most frequently isolated fungal organism worldwide. He recorded a 17 mm diameter inhibition zone at a concentration of 100 %. In addition, hydrolysed CU was most noted for its high ability to inhibit the growth of this fungus by creating an inhibition zone diameter of 20 mm, larger than that of raw urine (12 mm) (Khedr, 2016). This was confirmed by the survey of El-Desoukey (2020), where he accentuated the similar action of the antifungal Nystatin and CU on *C. albicans*. Undoubtedly, all the strains of this fungus in the study of Al-Awadi and Aljudaibi, (2014) were inhibited by fresh CU showing 44 mm, 40 mm and 37 mm after storage at 4 °C for 2, 4 and 6 months, respectively.

One of the most common sources of citric acid worldwide is *Aspergillus niger* (*A. niger*) since it releases proteases, lipases and amylases which are broadly employed in preparing beverages (Tong et al., 2019). Nonetheless, it can engender non-invasive aspergillosis, mainly otomycosis, which exists among 9 % to 30 % of patients having otitis externa (Opperman and Copelyn, 2020). Surely, by augmenting suspensions of CU from 25 % to 100 %, inhibition zones became bigger at a rate between 13 mm and 17 mm (Al-Bashan, 2011). Even at low concentrations from 3 % to 10 %, CU inhibited the mycelium growth of *A. niger* isolated from coffee beans on solid media by causing the analysis and plasmolysis of its hyphae (Al-Abdalall, 2010). Another study has documented that this microorganism was the most sensitive fungi tested by depicting an inhibition zone reaching 43 mm in the use of non-treated CU (Al-Awadi and Aljudaibi, 2014).

Aflatoxin B1 produced by *A. flavus* was the most powerful in comparison with other aflatoxins. As well, its high exposure is strongly associated with cirrhosis and mutations in the p53 tumour suppressor gene, which is the source of hepatocellular carcinoma, principally in immune-incompetent individuals (Aguilar et al., 1993). Equally, the trial realized by Khedr (2016) demonstrated that hydrolysed CU was superior (18 mm) to the fresh one (13 mm).

In the study performed by Kabbashi and Al Fadhil (2016), the investigators argued that CU inhibited around 100 % of dermatophyte growth, whilst fluconazole and ketoconazole drugs inhibited only around 80 % of these primary pathogens that were able to digest keratin found in nail, skin and hair (Monod, 2008). Starting with *Trichophyton rubrum*, the principal cause of tinea pedis and tinea unguium in developed countries was identified as the most sensitive fungus in this experiment, with an MIC equal to 1.25 µg/ml. El-Shahawy et al. (2010)

also validated the considerable antifungal effect of the extract PM701 on this pathogen (32 mm), comparing the inhibition zone, which was less than 20 mm for *Epidermophyton floccosum*, with an MIC corresponding to 6.25 µg/ml as the team of Kabbashi and Al Fadhil (2016) cited. Although *Microsporum canis* (*M. canis*) is known as the most common zoophilic dermatophyte, it was responsible for engendering tinea corporis and tinea capitis among humans (Pasquetti et al., 2017). The significance of the lyophilized form of CU PM701 was underscored by calculating a diameter of 30 mm. Congruently, the MIC at which 90 % of *M. canis* isolates were inhibited was 2.5 µg/ml (El-Shahawy et al., 2010, Kabbashi and Al Fadhil, 2016). Likewise, Kabbashi and Al Fadhil (2016) measured the following MICs: 1.25 µg/ml for both *Trichophyton mentagrophytes* and *Trichophyton tonsurans*, 0.312 µg/ml for *Microsporum gypseum* and 0.625 µg/ml for *Trichophyton violaceum*.

Aspergillus fumigatus (*A. fumigatus*) was an opportunistic pathogen, whereby humans were infected by inhaling spores called conidia. Systemic infections caused by this fungus were related with a high death rate mostly in people possessing weakened immune systems (Arastehfar et al., 2021). The Centers for Disease Control and Prevention (CDC) estimated that 19 % of *A. fumigatus* diseases are resistant to azole antifungals, which require a search for novel antifungal drugs. An Egyptian research team in association with Saudi Arabia stated that the powder of CU induced an inhibition zone of 22 mm (El-Shahawy et al., 2010).

At the agricultural level, Al-Abdalall (2010) displayed that *Rhizoctonia solani* isolated from fava beans and *Pythium aphanidermatum* isolated from mung beans were inhibited completely at 50 % of CU. Therefore, after the application of a titre of 25 % CU, he noticed the total inhibition of *Aschocayta* spp. in liquid and solid media, he also observed reductions in mycelial growth for *Sclerotinia sclerotiorum* and *Fusarium moniliform*.

F. oxysporum is a ubiquitous saprophyte in nature found in air, soil and on plants. It was able to produce an imbalance of the intestinal flora or mycotoxicosis in humans after ingesting contaminated food (Hof, 2020). It has been reported by Al-Awadi and Aljudaibi (2014) that a diameter of 39 mm against this fungus is possible using CU.

Osman et al. (2016) affirmed that CU produced a depletion in mycelia growth as well as in a colony's diameter for *Alternaria alternata*, which is the utmost cause of early blight, a devastating fungal disease in tomato. This decrease was in terms of increasing concentrations of CU from 5 % to 15 %.

3.8. Chemical compounds of CU as antimicrobials

From seventy-two chemicals found in CU by gas chromatography coupled with mass spectrometry (GC-MS), thirty-four were the deemed most significant to slow down the growth of microorganisms. Starting with the most representative bacteria, *E. coli* was sensitive to 14 chemicals. For instance, oxalic acid is effective against *E. coli*, exhibiting an MIC value of 0.3 mg/ml (Kwak et al., 2016) followed by canavanine, phenylacetic acid, glucuronolactone and butylparaben with an MIC of 0.5 mg/ml (Schwartz and Maas, 1960, Kim et al., 2004, Donaldson, 1951, Crovetto et al., 2017). For benzoic acid, urea, creatinine, lactic acid and valeric acid, the MIC values varied from 1.0 to 31 mg/ml (Synowiec et al., 2021, Kaye, 1968, McDonald et al., 2012, Stanojević-Nikolić et al., 2016, Kovanda et al., 2019). Four studies confirmed the *in vitro* effect against the same pathogen without mentioning the MICs of phenol, m-cresol, p-cresol and 2-deoxy-d-galactopyranose (Keweloh et al., 1990, Hartl et al., 2022, Passmore et al., 2018, TANAKA et al., 1994). Moving to gram-positive bacteria, *S. aureus* is more sensitive to 3-hydroxybenzoic acid and hydroxylamine with MICs both equal to 0.025 mg/ml (Ganesh et al., 2022, Tarr, 2011), while its value for linolenic acid was 1.0 mg/ml (Dilika et al., 2000). In addition, the inhibition of the same bacterial strain required 0.312 % acetic acid and 5 % ribitol (Fraise et al., 2013, Akiyama et al., 2002). In 2021, Casillas-Vargas et al. (2021) proved the antibacterial activity of palmitic acid against vancomycin-resistant *Enterococcus faecalis* by indicating an MIC value of 2

µg/ml, while its value for pseudouridine is in the range of 4–16 µg/ml (Maffioli et al., 2019). The hippuric acid was also active on the same pathogen (MIC = 89.58 µg/ml) (González De Llano et al., 2019).

L-alanine and malonic acid present in CU have also been recorded to possess antibacterial effects on *Edwardsiella tarda* and *Vibrio cholerae*, respectively (Peng et al., 2015, Minato et al., 2013). In 1993, it was observed that azelaic acid was efficacious against one of the parts of normal flora *Propionibacterium acnes* at the concentration MIC = 58.91 µg/ml (Holland and Bojar, 1993). Moreover, the inhibition of *M. tuberculosis* was noticed with the use of 40–100 µg/ml of cinnamic acid (Guzman, 2014). Also, elaidic acid and glycine were active against *Lactobacillus zeae* and *Helicobacter pylori*, exhibiting MIC values in the range of 0.5–2.5 mg/ml (Minami et al., 2004). The molecule (2S,3R)-butane-1,2,3,4-tetrol, which is known as erythritol, is also effective in the inhibition of the responsible agent of chronic periodontitis – *Porphyromonas gingivalis* – with an MIC equal to 64 mg/ml (Zhang et al., 2019). The antifungal activity in section 3.7 could be explained by the presence of many compounds in CU, such as salicylic acid, catechol, hydrocinnamic acid, 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione and o-cresol that have been reported to prevent the growth of fungi of medical interest, like *A. niger* (30.5 mm), *T. mentagrophytes* (25 mm) (Yiase et al., 2014), *F. oxysporum* (29.8 mm) (Kocaalişkan et al., 2006), *A. flavus* (3.90 to 15.62 µg/ml) (Yehia et al., 2020), *C. albicans* (Yadao, 2015) and *M. canis* (0.5 %) (Andersen, 2006). The metabolites present in CU and their effects against microorganisms have been assessed by disc or well diffusion methods and are listed in Table 2.

4. Discussion

This survey systematically reviewed current studies related to the antimicrobial activities of CU against microorganisms and evaluated the potential origins of its antimicrobial properties. CU has been widely known to possess diverse bioactive compounds used for the treatment of various diseases (Abdel Gader and Alhaider, 2016). Given its potent pharmaceutical values, it was underscored that CU is endowed with protective effects in liver toxicity and gastric ulcers, and it plays an important role as an antiplatelet agent as well (Salamt et al., 2021). Moreover, CU has an efficient cytotoxic effect against cancer cells (Al-Yousef et al., 2012). Despite its traditional use as a remedy in Sub-Saharan countries and in the Arabian Peninsula, it is necessary to standardize the effective dosage of CU by using a unique formulation in order to be used for treating different ailments. Additionally, a deep investigation would be essential to assess its potential side effects before considering it as an alternative treatment. To our knowledge, this is the first study to summarize data surrounding the antimicrobial effect of camel excretion.

As mentioned before, all the 19 papers included in the present review stated that CU has strong antibacterial, antiviral and antifungal activities against different pathogenic microorganisms without drawing attention to the mechanisms of action of this biofluid on the cell walls of bacteria or fungi. By using an electronic microscope, Shoeib (2008) was the first one who illustrated the mechanism of action of CU on some bacteria. He proved that CU caused abnormalities and crumpled to the cell walls of bacteria, which allowed for the penetration of antibiotics when the synergistic effect was tested. For gram-negative bacteria, he critically traces wrinkles in the *E. coli* cell wall after its treatment by CU in 24 h. Similarly, he argued that *P. aeruginosa* treated by this biofluid becomes shorter within one day and incurred the formation of wrinkles followed by cell death.

Furthermore, the antiviral activity of CU was explained by Noor et al. (2015) who demonstrated that CU induces the disintegration of viral epitopes followed by the inhibition of the virus' adsorption to the host cell. It was also proposed that CU produced a damage of viral proteins and affected virus replication too.

For the antifungal activity of CU, Al-Abdalall (2010) found that this excretion had many beneficial properties, specifically in the field of

agriculture, by preventing the generation of aflatoxins in the use of the agar pore technique. In addition, he recorded an important shrinkage in fungal growth as well as in the dry weight of the mycelial growth by enlarging the titres of the tested biofluid to 50 %.

These three antimicrobial activities could be attributed firstly to the consumption of salty desert plants, halophytes and thorny shrubs avoided by goats, cows and sheep. Nevertheless, the surveys conducted in Sudan and Egypt, (Elbehiry et al., 2021, Mostafa and Dwedar, 2016) illustrated that the origin of the antimicrobial properties of CU were accredited to some parts of wild plants such as *Convolvulus hystrix* Vahl, *Citrullus colocynthis* (L.) Schrad., *Haloxylon aphyllum* (Minkw.), *Aristida* L., *Salsola gemmascens* Pall., *Anabasis setigera*, *Astragalus* L., *Acacia pennata* subsp. *pennata*, *Vachellia flava* (Forssk.), *Dipterygium glaucum* Decne, *Salsola orientalis* S.G, *Rhazya stricta* Decne. and *Haloxylon persicum*. In addition to these plants and behind the climatic change in Saudi Arabia, Al-Bashan (2011) added other types of plants that camels were fed on: *Vachellia tortilis* subsp. *raddiana*, *Vachellia oerfota* var., *Vachellia tortilis* (Forssk.), *Vachellia seyal*, *Vachellia etbaica* (Schweinf.), *Vachellia farnesiana* (L.), *Rhanterium epapposum* Oliv., *Indigofera arabica*, *I. articulata*, *I. oblongifolia*, *I. tritoides*, *Rumex glaber*, *R. vesicarius*, *R. nepalensis*, *R. spinosus*, *Polycarpaea fragilis*, *P. repens*, *Ruellia patula*, *Ifloga spicata*, *Juncus acutus*, *J. rigidus*, *Heliotropium arbainense*, and *Herniaria cinerea*.

A colossal number of included studies have suggested that antimicrobial characteristics of CU were explained by its high alkalinity (pH ≥ 7.8) as an outcome of large amounts of potassium, magnesium and calcium, as well as the low percentage of cellulose and carbohydrates (Elbehiry et al., 2021, Mostafa and Dwedar, 2016, Sumia et al., 2016, Al-Bashan, 2011). Very recently, Ye et al. (2020) provided new evidence about zinc, which is one of the most important weapons against multidrug-resistant (MDR) bacteria. Its high rates lead to the inhibition of bacterial growth by protein denaturation, enzyme inactivation, alteration of the membrane and eventually cell death. Reyes-Jara et al. (2016) have also found that copper prevented the multiplication of microbial pathogens by inflicting membrane rupture for bacteria, damage of cellular morphology for fungi and RNA degradation for viruses. For this reason, Al Attas (2019) and El-Shahawy et al. (2010) interpreted the beneficial assets of CU by its richness of copper and zinc, which are the most important minerals in the lyophilized form of CU. To date, in the survey of Khedr (2016), it has been conclusively shown that CU contained immense proportions of azelaic acid and p-cresol, which were harmful to the growth of gram-negative bacteria and *Staphylococcus epidermidis*, respectively. They were considered as the causative agents of membrane cell disintegration (Passmore et al., 2018, Holland and Bojar, 1993).

Regarding the analytical chemistry of CU, seven scientific papers used only gas chromatography coupled with mass spectrometry (GC-MS) by including a derivatization step, which allows the discovery of 72 compounds that were believed to be present in significant amounts (Khorshid, 2016, Mahmoud et al., 2019, El-Nadi and Al-Torki, 2007; Salwa M.E. Khogali et al., 2011, Ahamad et al., 2017, Salwa et al., 2016, Emwas et al., 2015). This variability of compounds is due to diverse factors like sex, age, feeding, seasonality, metabolic pathways and gut microbiota (Iglesias Pastrana et al., 2022). However, more efforts are required to conduct further research in the future, namely by comparing the chemical attributes of each compound present in CU exhibiting diverse physiological statuses across various environmental, nutritional and management conditions. Furthermore, it is crucial to explore whether antimicrobial characteristics are inherent in the urine of all camels or if these properties are specific to camels with particular physiological and nutritional statuses.

In addition to anti-tumour, antioxidant and anti-inflammatory activities of chemical compounds found in this biofluid, thirty-four of them featured strong antimicrobial activity against microorganisms. The major chemicals identified in CU were phenolic acids (benzoic acid, cinnamic acid, hydro cinnamic acid and salicylic acid), phenols (o-cresol, p-cresol and m-cresol), and amino acids (glycine, l-alanine).

Table 2

Antimicrobial effects of chemicals found in camel urine.

Name of metabolite	IUPAC name	References	Antimicrobial activity (MIC/MBC/Diameter)	Concerned microorganism	References
Ethanoic acid	Acetic acid	(Salwa et al., 2016) (Emwas et al., 2015)	Minimal inhibitory concentration (MIC) MIC = 0.312 % MIC = 0.312 % MIC = 0.166 %	Methicilin-susceptible <i>Staphylococcus aureus</i> <i>Acinetobacter baumannii</i> <i>Pseudomonas aeruginosa</i> (PA)	(Fraise et al., 2013)
Glycine	2-Aminoacetic acid	(Emwas et al., 2015)	MIC = 2.5 mg/ml	<i>Helicobacter pylori</i>	(Minami et al., 2004)
N-phenylacetyl glycine	2-(N-Acetylanilino)acetate	(Mahmoud et al., 2019) (Ahamad et al., 2017)	Not mentioned	Not mentioned	Not mentioned
Aminomalonic acid	2-Aminopropanedioic acid	(Ahamad et al., 2017) (Mahmoud et al., 2019)	Not mentioned	Not mentioned	Not mentioned
Canavanine	(2S)-2-Amino-4-(diaminomethylidene aminoxy)butanoic acid	(Ahamad et al., 2017) (Mahmoud et al., 2019)	MIC = 500 µg/ml	<i>Escherichia coli</i> (E. coli)	(Schwartz & Maas, 1960)
Creatinine	2-Amino-3-methyl-4H-imidazol-5-one	(Ahamad et al., 2017) (Mahmoud et al., 2019)	MIC = 5.98 mg/ml MIC = 2.24 mg/ml	<i>E. coli</i> <i>Staphylococcus aureus</i> (S. aureus)	(McDonald et al., 2012)
L-alanine	(2S)-2-Aminopropanoic acid	(Read, 1925) (Emwas et al., 2015)	Not mentioned	<i>Edwardsiella tarda</i>	(Peng et al., 2015)
Hippuric acid	2-Benzamidoacetic acid	(Emwas et al., 2015) (Ahamad et al., 2017) (Mahmoud et al., 2019) (Read, 1925)	89.58 µg/ml	<i>Enterococcus faecalis</i> (E. faecalis)	(González De Llano et al., 2019)
Catechol	Benzene-1,2-diol	(Emwas et al., 2015)	31.3 mm 29.8 mm 26.5 mm	<i>Pseudomonas putida</i> <i>Fusarium oxysporum</i> <i>Penicillium italicum</i>	(Kocaçalışkan et al., 2006)
Benzoic acid	Benzoic acid	(Salwa et al., 2016) (Emwas et al., 2015)	MIC = 1 mg/ml	<i>E. coli</i>	(Synowiec et al., 2021)
Erythritol	(2S,3R)-Butane-1,2,3,4-tetrol	(Mahmoud et al., 2019) (Emwas et al., 2015) (Ahamad et al., 2017)	MIC = 64 g/l MIC = 128 g/l MIC = 128 g/l	<i>Porphyromonas gingivalis</i> <i>Aggregatibacter actinomycetemcomitans</i> <i>Actinomyces viscosus</i>	(Zhang et al., 2019)
Butyl butyrate	Butyl butanoate	(Salwa et al., 2016)	Not mentioned	Not mentioned	Not mentioned
Butylparaben	Butyl 4-hydroxybenzoate	(Salwa et al., 2016)	Minimal bactericidal concentration (MBC) MBC = 5 mg/ml MBC = 10 mg/ml	<i>E. coli</i> <i>S. aureus</i>	(Crovetto et al., 2017)
Butyl palmitate	Butyl hexadecanoate	(Salwa M.E. Khogali et al., 2011)	Not mentioned	Not mentioned	Not mentioned
Bicyclo[4.2.0]octa-1,3,5-triene-7-carboxylic acid	Bicyclo [4.2.0]octa-1,3,5-triene	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned

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Table 2 (continued)

Name of metabolite	IUPAC name	References	Antimicrobial activity (MIC/MBC/Diameter)	Concerned microorganism	References
5,6,7,8-Tetrahydridibenz-[c,e]azocine	9-Azatricyclo [10.4.0.0.2,7]-hexadeca-1 (16),2,4,6,12,14-hexaene	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
Naphtho[2,3-b]thiophene	Benzo[f][1]benzothiole	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
Creatine	2-[carbamidimidoyl(methyl)-amino]acetic acid	(Read, 1925)	Not mentioned	Not mentioned	Not mentioned
1,2-Dichloro-4-ethylbenzene	1,2-Dichloro-4-ethylbenzene	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
Glucuronolactone	(2R)-2-[(2S,3R,4S)-3,4-Dihydroxy-5-oxoxolan-2-yl]-2-Hydroxyacetaldehyde	(Ahamad et al., 2017) (Mahmoud et al., 2019)	MIC = 0.5 à 2 %	<i>E. coli</i>	(Donaldson & Bricker, 1951)
1,2,3,4,6,7,8,11,-12,12b-Decahydrobenzo-[a]anthracene	1,2,3,4,6,7,8,11,12,12b-Decahydrobenzo-[a]anthracene	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
Lageracetal	1,1-Dibutoxybutane	(Salwa M.E. Khogali et al., 2011) (Salwa et al., 2016)	Not mentioned	Not mentioned	Not mentioned
2-Chlorosantonin	(3S,3aS,5aS,9bS)-7-Chloro-3,5a,9-trimethyl-3a,4,5,9b-tetrahydro-3H-benzo [g][1]benzofuran-2,8- dione	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
Uric acid	7,9-Dihydro-3H-purine-2,6,8-trione	(Emwas et al., 2015)	Not mentioned	Not mentioned	Not mentioned
D-Talofuranose	(3S,4R,5S)-5-[(1R)-1,2-Dihydroxyethyl]oxolane-2,3,4-triol	(Emwas et al., 2015)	IC50 = 0.90 µg/ml	Gram-positive bacteria	(Ichikawa & Matsuda, 2007)
2,9-Dimethyl-5,6,11,12-tetrahydro-dibenzo-(A,E) cyclooctene	6,15-Dimethyltricyclo [10.4.0.0.4,9] hexadeca-1(12),4(9),5,7,13,15-hexaene	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
1,1-Diphenyl-1-propene-2-thiol	1,1-Diphenyl-1-propene-2-thiol	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
Pyrazine, 2,5-dimethyl-, 1,4-dioxide	2,5-Dimethyl-4-oxidopyrazin-1-ium 1-oxide	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
Prostaglandin F1a	7-[3,5-Dihydroxy-2-(3-hydroxyoct-1-enyl)cyclopentyl]-heptanoic acid	(Ahamad et al., 2017) (Mahmoud et al., 2019)	Not mentioned	Not mentioned	Not mentioned
Pseudouridine	5-[(2S,3R,4S,5R)-3,4-Dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1H-pyrimidine-2,4-dione	(Ahamad et al., 2017) (Mahmoud et al., 2019) (Emwas et al., 2015)	MIC = 4 à 6 µg/ml MIC = 4 à 16 µg/ml	<i>Streptococcus</i> spp <i>Staphylococcus</i> and <i>Enterococcus</i> spp.	(Maffioli et al., 2019)
D-Galactose	(3R,4S,5R,6R)-6-(Hydroxymethyl)oxane-2,3,4,5-tetrol	(Ahamad et al., 2017) (Mahmoud et al., 2019)	Not mentioned	Not mentioned	Not mentioned
Palmitic Acid	Hexadecanoic acid	(Ahamad et al., 2017) (Mahmoud et al., 2019)	MIC = 0.5 µg/mL MIC = 2 µg/mL	<i>Staphylococcus epidermidis</i> <i>E. faecalis</i>	(Casillas-Vargas et al., 2021)
2-Deoxy-D-galactopyranose	(4R,5R,6R)-6-(Hydroxymethyl)oxane-2,4,5-triol	(Ahamad et al., 2017) (Mahmoud et al., 2019)	Not mentioned	<i>E. coli</i>	(Tanaka et al., 1994)
Lactic acid	2-Hydroxypropanoic acid	(Emwas et al., 2015)	MIC = 1.25 mg/ml MIC = 1.25 mg/ml MIC = 2.5 mg/ml MIC = 2.5 mg/ml MIC = 1.25 mg/ml MIC = 2.5 mg/ml MIC = 2.5 mg/ml	PA <i>Salmonella enteritidis</i> <i>Proteus mirabilis</i> <i>E.coli</i> <i>Listeria monocytogenes</i> <i>S.aureus</i> <i>E. faecalis</i>	(Stanojević-Nikolić et al., 2016)

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Table 2 (continued)

Name of metabolite	IUPAC name	References	Antimicrobial activity (MIC/MBC/Diameter)	Concerned microorganism	References
2-Hydroxyisobutyric acid	2-Hydroxy-2-methylpropanoic acid	(Emwas et al., 2015)	Not mentioned	Not mentioned	Not mentioned
beta-Hydroxyisovaleric acid	3-Hydroxy-3-methylbutanoic acid	(Emwas et al., 2015)	Not mentioned	Not mentioned	Not mentioned
Salicylic acid	2-Hydroxybenzoic acid	(Salwa M.E. Khogali et al., 2011) (Emwas et al., 2015)	30.5 mm > 30 > 25 mm	<i>Aspergillus niger</i> > <i>Aspergillus hereus</i> > <i>Trichophyton mentagrophytes</i>	(Yiase et al., 2014)
3-Hydroxybenzoic acid	3-Hydroxybenzoic acid	(Emwas et al., 2015)	25 µg/ml (90.34 % biofilm formation)	<i>S. aureus</i>	(Ganesh et al., 2022)
3-(3-Hydroxyphenyl)-3-hydroxypropanoic acid	3-Hydroxy-3-(3-hydroxyphenyl) propanoic acid	(Emwas et al., 2015)	Not mentioned	Not mentioned	Not mentioned
Pimelic acid	Heptanedioic acid	(Emwas et al., 2015)	Not mentioned	Not mentioned	Not mentioned
Salicyluric acid	2-[(2-Hydroxybenzoyl)-amino]acetic acid	(Emwas et al., 2015)	Not mentioned	Not mentioned	Not mentioned
Hydroxylamine	Hydroxylamine	(Salwa et al., 2016)	25 µg/mL	<i>S. aureus</i> <i>Clostridium botulinum</i>	(Tarr, 2011)
1-(2-Hydroxyphenyl)-3-phenylpropane-1,3-dione	1-(2-Hydroxyphenyl)-3-phenylpropane-1,3-dione	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	<i>Aspergillus niger</i> <i>Candida albicans</i>	(Yadao, 2015)
2-(Methylthio)phenyl isothiocyanate	1-Isothiocyanato-2-methylsulfanylbenezene	(Salwa et al., 2016)	Not mentioned	Not mentioned	Not mentioned
Methylsuccinic acid	2-Methylbutanedioic acid	(Mahmoud et al., 2019) (Ahamad et al., 2017)	Not mentioned	Not mentioned	Not mentioned
O-cresol	2-methylphenol	(Emwas et al., 2015)	0.5 %	<i>Microsporum canis</i>	(Andersen, 2006)
M-cresol	3-methylphenol	(Emwas et al., 2015)	Not mentionned	<i>E. coli</i>	(Hartl et al., 2022)
P-cresol	4-methylphenol	(Emwas et al., 2015)	Not mentionned	<i>E. coli</i> , <i>Klebsiella oxytoca</i> and <i>Proteus mirabilis</i>	(Passmore et al., 2018)
3-methylheptan-4-one	3-methylheptan-4-one	(Salwa et al., 2016)	Not mentioned	Not mentioned	Not mentioned
9-Methylantracene	9-Methylantracene	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
Retene	1-Methyl-7-propan-2-ylphenanthrene	(Salwa et al., 2016)	Not mentioned	Not mentioned	Not mentioned
3-Methyladipic acid	3-Methylhexanedioic acid	(Emwas et al., 2015)	Not mentioned	Not mentioned	Not mentioned
1-Methyl-1H-imidazol-2-amine	1-Methylimidazol-2-amine	(Emwas et al., 2015)	Not mentioned	Not mentioned	Not mentioned
2,3-Dicyano-5-methyl-6-phenylpyrazine	5-Methyl-6-phenylpyrazine-2,3-dicarbonitrile	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
4-Methyldiben-zothiophene	4-Methyldibenzothiophene	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
1-Methylxanthine	1-Methyl-3,7-dihydropurine-2,6-dione	(A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned	Not mentioned	Not mentioned
Azelaic acid	Nonanedioic acid	(Ahamad et al., 2017) (Mahmoud et al., 2019)	40 µg/ml 100 µg/ml	<i>Propionibacterium acnes</i> <i>Staphylococcus epidermidis</i>	(Holland & Bojar, 1993)
Elaidic acid	(E)-Octadec-9-enoic acid	(Salwa M.E. Khogali et al., 2011) (Mahmoud et al., 2019) (Ahamad et al., 2017)	MIC = 500 mg/l	<i>Lactobacillus zeae</i>	(Wu & Shah, 2014)
Oxalic acid	Oxalic acid	(Emwas et al., 2015)	MIC = 250 mg/l MIC = 300 mg/l	<i>Ralstonia solanacearum</i> <i>Pectobacterium carotovorum</i> <i>Agrobacterium tumefaciens</i> <i>Xanthomonas axonopodis</i> <i>E. coli</i>	(Kwak et al., 2016)

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Table 2 (continued)

Name of metabolite	IUPAC name	References	Antimicrobial activity (MIC/MBC/Diameter)	Concerned microorganism	References
Linolenic acid	(9Z,12Z,15Z)-octadeca-9,12,15-trienoic acid	(Salwa et al., 2016)	MIC = 0.01 mg/ml MIC = 0.01 mg/ml MIC = 1 mg/ml MIC = 1 mg/ml	<i>Bacillus cereus</i> <i>Bacillus subtilis</i> <i>Bacillus pumilus</i> <i>Micrococcus kristinae</i> <i>S. aureus</i>	(Dilika et al., 2000)
Malonic acid	Propanedioic acid	(Ahmad et al., 2017) (Mahmoud et al., 2019)	Not mentioned	<i>Vibrio cholerae</i>	(Minato et al., 2013)
Ribitol/Xylitol	(2S,4R)-Pentane-1,2,3,4,5-pentol	(Mahmoud et al., 2019) (Ahmad et al., 2017)	5 % of Xylitol	<i>S. aureus</i>	(Akiyama et al., 2002)
Hydrocinnamic acid	3-Phenylpropanoic acid	(Mahmoud et al., 2019)	3.90 to 15.62 µg/ml	<i>Xanthomonas</i> <i>Oryzae</i> <i>Pseudomonas syringae</i> <i>Aspergillus flavus</i> <i>Fusarium solani</i>	(Yehia et al., 2020)
Phenylacetic acid	2-Phenylacetic acid	(Emwas et al., 2015)	13.2 mm (500 µg/ml) 13.7 mm (500 µg/ml)	<i>S. aureus</i> KCTC 1928 <i>E. coli</i> ATCC 10536	(Kim et al., 2004)
Valeric acid	Pentanoic acid	(Salwa et al., 2016)	2000 to 2800 mg/l 500 to 1000 mg/l	<i>E. coli</i> <i>Salmonella</i> <i>Typhimurium</i> <i>Campylobacter jejuni</i> <i>E. coli</i>	(Kovanda et al., 2019)
Phenol	Phenol	(Salwa M.E. Khogali et al., 2011)	Not mentioned	<i>Mycobacterium tuberculosis</i> H ₃₇ Rv	(Keweloh et al., 1990)
Cinnamic acid	(E)-3-phenylprop-2-enoic acid	(Salwa M.E. Khogali et al., 2011)	270–675 µM		(Guzman, 2014)
p-cresol glucuronide	(2S,3S,4S,5R,6S)-3,4,5-trihydroxy-6-(4-methylphenoxy) oxane-2-carboxylic acid	(Emwas et al., 2015) (Salwa M.E. Khogali et al., 2011)	Not mentioned	Not mentioned	Not mentioned
D-Galacturonic acid	(2S,3R,4S,5R)-3,4,5,6-Tetrahydroxyoxane-2-carboxylic acid	(Emwas et al., 2015)	Not mentioned	Not mentioned	Not mentioned
Propane, 1,2-bis (difluoroamino)-2-methyl-2,3,5-Trimethylphenanthrene	1-N,1-N,2-N,2-N-Tetrafluoro-2-methylpropane-1,2-diamine 2,3,5-Trimethylphenanthrene	(Salwa et al., 2016) (A. H. El-Nadi & A.I Al-Torki, 2007)	Not mentioned Not mentioned	Not mentioned Not mentioned	Not mentioned Not mentioned
Urea	Urea	(Read, 1925) (Emwas et al., 2015)	3.1 to 6.3 g/100 ml	<i>E. coli</i>	(Kaye, 1968)

Other constituents such as polyunsaturated fatty acids, represented mainly by linoleic acid, and palmitic acid were also among the most notable group of chemicals found in CU. All the previous studies have a

significant drawback as they failed to provide precise quantification data. In this context, the detection of a large number of metabolites and new bioactive compounds needs more complementary methodologies

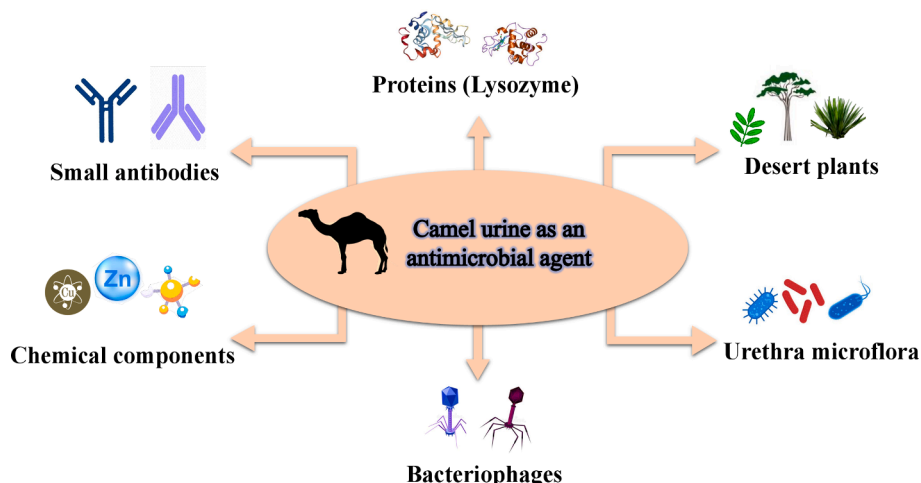


Fig. 3. Sources of antimicrobial properties of camel urine.

like nuclear magnetic resonance (NMR) and liquid chromatography-mass spectrometry (LC-MS), as well as the fractionation of CU to extract and purify the active natural molecules in this biofluid.

Among the other explanations of antimicrobial properties, Noor et al. (2015) elucidated the antimicrobial effects of CU by the lysozyme enzyme; it is responsible for hydrolysis of peptidoglycan's constituents, principally gram-positive bacteria. Nonetheless, data from these three studies (A-Ameri et al., 2015, Al-Bashan, 2011, Humaid, 2016) spelled out the benefits of CU by the presence of lytic and temperate bacteriophages, which was even upheld by Żaczek et al. (2020) in human urine. Additionally, researchers have found that antibodies were also involved in the composition of CU in order to combat bacteria and fungi by neutralization and viruses by preventing their entrance to the target cells (Humaid, 2016, Shinashal, 2014). As a final suggestion, it is vital to mention that CU naturally contained bacteria that were able to produce anti-bacterial substances (Al-Bashan, 2011, A-Ameri et al., 2015, Al-Awadi and Aljudaibi, 2014). Fig. 3 shows a graphic representation of different sources of antimicrobial characteristics of CU. Noteworthy, CU should be further investigated to unveil the exact mechanism beyond the antimicrobial effect of its individual compounds and then discover multiple pathways to be targeted. Official, standardized methods for establishing this activity efficiently are in high demand.

5. Conclusions

The current review attempted to shed light on the wide use of CU against microorganisms, which dates back over a century in the treatment of various infectious illnesses, namely tuberculosis, acne and ringworm. Mostly, it is an excellent candidate for the development of antimicrobial drugs. Nevertheless, the limited number of papers published on this topic have predominantly originated only from a few Arabian countries. Thus, numerous research groups in Europe or the United States have the option to develop these capabilities internally or engage in collaborative efforts with other groups to exchange expertise. These collaborations facilitate a more profound exploration of biodiversity and enable the sharing of specialized knowledge. Comprehensive surveys are required to explore synergistic interactions within CU and between its active ingredients and antibiotics or antifungals in order to bring out the hidden processes behind the antimicrobial properties of its composites and then uncover multiple pathways to pursue. Additionally, the responsible components of the antimicrobial activity varied in all the included studies. There is a need for more well-designed scrutiny incorporating *in vitro* testing of each isolated compound of CU on microbes by using standardized methods as well as *in vivo* clinical trials in experimental models of infection to ensure its biosafety and clinical effectiveness in pharmaceutical applications. In this context, further research should focus on elaborating databases and big collections of bioactive chemicals of CU and all the camel-derived products to be generalized and standardized internationally.

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CRedit authorship contribution statement

Ressmi Amina: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization, Funding acquisition, Project administration and Software.
Raqraq Habiba: Resources, Investigation, Data curation, Software.
Barguigua Abouddihaj: Writing – review & editing, Validation, Supervision, Project administration, Methodology, Conceptualization, Visualisation, Project administration and Software.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- A-Ameri, G.A., Alkolaibe, A.M., Al-kadassy, A.M., Alkadasi, M.N., Zaide, A.A., 2015. Determination the efficiency of camel's urine against multi-drugs resistant *Pseudomonas aeruginosa* (MDRPA), isolated from effected burns, wounds and ears. *Asian Jour. Pharmac. Res.* 5, 1. Doi: 10.5958/2231-5691.2015.00001.5.
- Abdalla, I., Haroun, E., Hayder, Abdalla, 2018. Effects of type of nutrition on the chemical composition of camels milk and urine. *Gezira J. Agric. Sci.* 16.
- Abdalla, O.M., Wasfi, I.A., Gadir, F.A., 1988. The arabian race camel normal parameters—I. Haemogram, enzymes and minerals. *Comp. Biochem. Physiol. A Physiol.* 90, 237–239. [https://doi.org/10.1016/0300-9629\(88\)91110-3](https://doi.org/10.1016/0300-9629(88)91110-3).
- Abdel Gader, A.G.M., Alhaider, A.A., 2016. The unique medicinal properties of camel products: A review of the scientific evidence. *J. Taibah Univ. Med. Sci.* 11, 98–103. <https://doi.org/10.1016/j.jtumed.2015.12.007>.
- Abdullahi, A., Berhane, N., Zemene, A., 2021. Evaluation of In-Vitro Anti-Bacterial Qualities of Camels Urine in Somali Region of Ethiopia against Selected Bacterial Pathogens. *Int. J. Biotechnol.* 10, 1–14. <https://doi.org/10.18488/journal.57.2021.101.1.14>.
- Aguilar, F., Hussain, S.P., Cerutti, P., 1993. Aflatoxin B1 induces the transversion of G→T in codon 249 of the p53 tumor suppressor gene in human hepatocytes. *Proc. Natl. Acad. Sci. USA* 90, 8586–8590. <https://doi.org/10.1073/pnas.90.18.8586>.
- Ahamad, S.R., Alhaider, A.Q., Raish, M., Shakeel, F., 2017. Metabolomic and elemental analysis of camel and bovine urine by GC-MS and ICP-MS. *Saudi. J. Biol. Sci.* 24, 23–29. <https://doi.org/10.1016/j.sjbs.2015.09.001>.
- Akiyama, H., Oono, T., Huh, W.-K., Yamasaki, O., Ogawa, S., Katsuyama, M., Ichikawa, H., Iwatsuki, K., 2002. Actions of Farnesol and Xylitol against *Staphylococcus aureus*. *Chemotherapy* 48, 122–128. <https://doi.org/10.1159/000064916>.
- Al Attas, S.A., 2019. Antiviral activity of extracted fraction from camel urine against Corona and Influenza A (H1N1) viruses. *Appl. Ecol. Env. Res.* 17 https://doi.org/10.15666/aer/1705_1102311031.
- Al-Abdalall, A.H.A., 2010. The inhibitory effect of camel's urine on mycotoxins and fungal growth. *Afr. J. Agric. Res.* 5, 1331–1337.
- AlAwadi, A., Aljudaibi, A., 2014. Effects of Heating and Storage on the Antifungal Activity of Camel Urine. *Clin. Microbiol.* 03 <https://doi.org/10.4172/2327-5073.1000179>.
- Al-Awadi, A., Aljudaibi, A., 2014. Effects of Heating and Storage on the Antifungal Activity of Camel Urine. *Clin. Microbiol.: Open Access* 3. <https://doi.org/10.4172/2327-5073.1000179>.
- Al-Bashan, M.M., 2011. In vitro assessment of the antimicrobial activity and biochemical properties of camel's urine against some human pathogenic microbes. *Middle East J. Sci. Res.* 7, 947–958.
- Ali, A., Baby, B., Vijayan, R., 2019. From Desert to Medicine: A Review of Camel Genomics and Therapeutic Products. *Frontiers in Genetics* 10.
- Als, D., Radhakrishnan, A., Arora, P., Gaffey, M.F., Campisi, S., Velummailum, R., Zareef, F., Bhutta, Z.A., 2018. Global Trends in Typhoidal Salmonellosis: A Systematic Review. *Am. J. Trop. Med. Hyg.* 99, 10–19. <https://doi.org/10.4269/ajtmh.18-0034>.
- Al-Yousef, N., Gaafar, A., Al-Otaibi, B., Al-Jammaz, I., Al-Husseini, K., Aboussekhra, A., 2012. Camel urine components display anti-cancer properties in vitro. *J. Ethnopharmacol.* 143, 819–825. <https://doi.org/10.1016/j.jep.2012.07.042>.
- Al-Zahrani, S., Al-Harbi, A., 2011. Antimicrobial Activity of Camel's Urine on Methicillin-Resistant *Staphylococcus aureus* Isolated from Clinical Specimens. *J. King Abdulaziz Univ.-Sci.* 23, 251–268. <https://doi.org/10.4197/sci.23.1.16>.
- Andersen, A., 2006. Final report on the safety assessment of sodium p-chloro-m-cresol, p-chloro-m-cresol, chlorothymol, mixed cresols, m-cresol, o-cresol, p-cresol, isopropyl cresols, thymol, o-cymen-5-ol, and carvacrol. *Int. J. Toxicol.* 25 (Suppl 1), 29–127. <https://doi.org/10.1080/10915810600716653>.
- Arastehfar, A., Carvalho, A., Houbaken, J., Lombardi, L., Garcia-Rubio, R., Jenks, J.D., Rivero-Menendez, O., Aljohani, R., Jacobsen, I.D., Berman, J., Osherov, N., Hedayati, M.T., Ilkit, M., Armstrong-James, D., Gabaldón, T., Meletiadis, J., Kostezwa, M., Pan, W., Lass-Flörl, C., Perlin, D.S., Hoenigl, M., 2021. *Aspergillus fumigatus* and aspergillosis: From basics to clinics. *Stud. Mycol.* 100, 100115 <https://doi.org/10.1016/j.simyco.2021.100115>.
- Bakhsh, R.S., Noor, S.O., Khorshid, F.A.R., Ahmed, F., Alsulaimany, A.A., Najjar, A.A., Al-Hejin, A.M., 2019. The antibacterial activity of a fraction extracted from camel urine against mycobacterium tuberculosis isolated from tuberculosis patients in Jeddah City. *Adv. Environ. Biol.* 13, 1–6. <https://doi.org/10.22587/aeb.2019.13.4.1>.
- Bass, N.M., Williams, R.L., 1988. Guide to drug dosage in hepatic disease. *Clin. Pharmacokinet.* 15, 396–420. <https://doi.org/10.2165/00003088-198815060-00004>.
- Bayed, J., Issa, M., El Fadil, A., 2020. Susceptibility pattern in pathogenic bacteria isolated from clinical specimens of wounds antimicrobial effects of camel's urine compared with antibiotic.
- Behzadi, P., Baráth, Z., Gajdacs, M., 2021. It's Not Easy Being Green: A Narrative Review on the Microbiology, Virulence and Therapeutic Prospects of Multidrug-Resistant

- Pseudomonas aeruginosa*. *Antibiotics* (basel) 10, 42. <https://doi.org/10.3390/antibiotics10010042>.
- Casillas-Vargas, G., Ocasio-Malavé, C., Medina, S., Morales-Guzmán, C., Del Valle, R.G., Carbalreira, N.M., Sanabria-Ríos, D.J., 2021. Antibacterial fatty acids: An update of possible mechanisms of action and implications in the development of the next-generation of antibacterial agents. *Prog. Lipid Res.* 82, 101093 <https://doi.org/10.1016/j.plipres.2021.101093>.
- Clegg, S., Murphy, C.N., 2016. Epidemiology and Virulence of *Klebsiella pneumoniae*. *Microbiol. Spectr.* 4, 4.1.06. <https://doi.org/10.1128/microbiolspec.UTI-0005-2012>.
- Crovetto, S.I., Moreno, E., Dib, A.L., Espigares, M., Espigares, E., 2017. Bacterial toxicity testing and antibacterial activity of parabens. *Toxicol. Environ. Chem.* 99, 858–868. <https://doi.org/10.1080/02772248.2017.1300905>.
- Dilika, F., Bremner, P.D., Meyer, J.J.M., 2000. Antibacterial activity of linoleic and oleic acids isolated from *Helichrysum pedunculatum*: a plant used during circumcision rites. *Fitoterapia* 71, 450–452. [https://doi.org/10.1016/S0367-326X\(00\)00150-7](https://doi.org/10.1016/S0367-326X(00)00150-7).
- Donaldson, R.C., 1951. Use of glucuronolactone with streptomycin for reducing bacterial flora of the colon. *Arch. Surg.* 62, 118. <https://doi.org/10.1001/archsurg.1951.01250030121013>.
- Elbehry, A., Marzouk, E., Moussa, I.M., Alenzi, A., Al-Maary, K.S., Mubarak, A.S., Alshammari, H.D., Al-Sarar, D., Alsubki, R.A., Hemeg, H.A., Kabli, S.A., Attala, O.A., 2021. Multidrug-resistant *Escherichia coli* in Raw Milk: Molecular Characterization and the potential impact of camel's Urine as an Antibacterial Agent. *Saudi J. Biol. Sci.* 28, 2091–2097. <https://doi.org/10.1016/j.sjbs.2021.01.018>.
- El-Desoukey, R.M.A., 2020. Comparative Antimicrobial Study of Camel Milk and Urine against Some Animal Patho-gens. *EC Vet. Sci.* 5, 134–141.
- El-Nadi, A.H., Al-Torki, A.I., 2007. Chemical and biochemical composition of pregnant camel urine (Camelus dromedarius).
- El-Shahawy, A., Elsayi, N.M., Baker, W.S., Khorshid, F., Geweely, N.S., 2010. Antimicrobial Activity of PMF-G Fraction extracted from PM-701. *Int. J. Pharm. Bio. Sci.* 1.
- Emwas, A.-H., Al-Talla, Z., Kharbatia, N., 2015. Sample Collection and Preparation of Biofluids and Extracts for Gas Chromatography–Mass Spectrometry. *Methods in molecular biology* (Clifton, N.J.) 1277, 75–90. https://doi.org/10.1007/978-1-4939-2377-9_7.
- Fraise, A.P., Wilkinson, M.A.C., Bradley, C.R., Oppenheim, B., Moiem, N., 2013. The antibacterial activity and stability of acetic acid. *J. Hosp. Infect.* 84, 329–331. <https://doi.org/10.1016/j.jhin.2013.05.001>.
- Ganesh, P.S., Veena, K., Senthil, R., Iswamy, K., Ponmalar, E.M., Mariappan, V., Girija, A.S.S., Vadivelu, J., Nagarajan, S., Challabathula, D., Shankar, E.M., 2022. Biofilm-Associated Agr and Sar Quorum Sensing Systems of *Staphylococcus aureus* are Inhibited by 3-Hydroxybenzoic Acid Derived from *Illicium verum*. *ACS Omega* 7, 14653–14665. <https://doi.org/10.1021/acsomega.1c07178>.
- Gole, F., 2020. Review on Health Benefits of Camel Urine: Therapeutics Effects and Potential Impact on Public Health Around East Hararghe District. *Am. J. Pure Appl. Biosci.* 2, 183–191. <https://doi.org/10.34104/ajpab.020.01830191>.
- González De Llano, D., Liu, H., Khoo, C., Moreno-Arribas, M.V., Bartolomé, B., 2019. Some New Findings Regarding the Antidhesive Activity of Cranberry Phenolic Compounds and Their Microbial-Derived Metabolites against Uropathogenic Bacteria. *J. Agric. Food Chem.* 67, 2166–2174. <https://doi.org/10.1021/acs.jafc.8b05625>.
- Guzman, J.D., 2014. Natural Cinnamic Acids, Synthetic Derivatives and Hybrids with Antimicrobial Activity. *Molecules* 19, 19292–19349. <https://doi.org/10.3390/molecules191219292>.
- Hartl, H., Li, W., Michl, T.D., Anangi, R., Speight, R., Vasilev, K., Ostrikov, K.K., MacLeod, J., 2022. Antimicrobial adhesive films by plasma-enabled polymerisation of m-cresol. *Sci Rep* 12, 7560. <https://doi.org/10.1038/s41598-022-11400-8>.
- Hof, H., 2020. The Medical Relevance of Fusarium spp. *J. Fungi* (basel) 6, E117. <https://doi.org/10.3390/jof6030117>.
- Holland, K., Bojar, R., 1993. Antimicrobial effects of azelaic acid. *J. Dermatol. Treat.* 4, S8–S11. <https://doi.org/10.3109/09546639309082152>.
- Humaid, A.A., 2016. Antagonistic effect of camel's urine on some pathogenic bacterial species. *PSM Vet. Res.* 1, 08–12.
- Iglesias Pastrana, C., Delgado Bermejo, J.V., Sgobba, M.N., Navas González, F.J., Guerra, L., Pinto, D.C.G.A., Gil, A.M., Duarte, I.F., Lentini, G., Ciani, E., 2022. Camel (*Camelus* spp.) Urine Bioactivity and Metabolome: A Systematic Review of Knowledge Gaps, Advances, and Directions for Future Research. *Int. J. Mol. Sci.* 23, 15024. <https://doi.org/10.3390/ijms232315024>.
- Ioannou, P., Vamvoukaki, R., Kofteridis, D.P., 2022. Infective endocarditis by *Enterobacter cloacae*: a systematic review and meta-analysis. *J. Chemother.* 34, 1–8. <https://doi.org/10.1080/1120009X.2021.1959786>.
- Kabbashi, M.A., Al Fadhil, A.O., 2016. In vitro Antifungal Activity of Camel's Urine against Dermatophytes.
- Kaper, J.B., Nataro, J.P., Mobley, H.L.T., 2004. Pathogenic *Escherichia coli*. *Nat. Rev. Microbiol.* 2, 123–140. <https://doi.org/10.1038/nrmicro818>.
- Kaye, D., 1968. Antibacterial activity of human urine. *J. Clin. Invest.* 47, 2374–2390.
- Keweloh, H., Weyrauch, G., Rehm, H.-J., 1990. Phenol-induced membrane changes in free and immobilized *Escherichia coli*. *Appl. Microbiol. Biotechnol.* 33, 66–71. <https://doi.org/10.1007/BF00170572>.
- Khedr, A., 2016. Characterization and Determination of Major Bioactive Acids in Camel Urine Using Gas Chromatography Mass-spectrometry. *IJPS* 78. <https://doi.org/10.4172/pharmaceutical-sciences.1000168>.
- Salwa, M.E. Khogali, Samia H. Abdalrahman, Esraa M. Musa, Abdalla M. El Hassan, 2011. Gas chromatography mass spectrophotometry (gc-ms) analysis of female camel urine extracts.
- Khorshid, F., 2016. Characterization and Determination of Major Bioactive Acids in Camel Urine Using Gas Chromatography Massspectrometry. *Indian J. Pharm. 78*.
- Kim, Y., Cho, J.-Y., Kuk, J.-H., Moon, J.-H., Cho, J.-I., Kim, Y.-C., Park, K.-H., 2004. Identification and Antimicrobial Activity of Phenylacetic Acid Produced by *Bacillus licheniformis* Isolated from Fermented Soybean. *Chungkook-Jang. Curr. Microbiol.* 48, 312–317. <https://doi.org/10.1007/s00284-003-4193-3>.
- Kocaçalışkan, I., Talan, I., Terzi, I., 2006. Antimicrobial Activity of Catechol and Pyrogallol as Allelochemicals. *Zeitschrift Für Naturforschung C* 61, 639–642. <https://doi.org/10.1515/znc-2006-9-1004>.
- Kovanda, L., Zhang, W., Wei, X., Luo, J., Wu, X., Atwill, E.R., Vaessen, S., Li, X., Liu, Y., 2019. In Vitro Antimicrobial Activities of Organic Acids and Their Derivatives on Several Species of Gram-Negative and Gram-Positive Bacteria. *Molecules* 24, 3770. <https://doi.org/10.3390/molecules24203770>.
- Kwak, A.-M., Lee, I.-K., Lee, S.-Y., Yun, B.-S., Kang, H.-W., 2016. Oxalic Acid from *Lentinula edodes* Culture Filtrate: Antimicrobial Activity on Phytopathogenic Bacteria and Qualitative and Quantitative Analyses. *Mycobiology* 44, 338–342. <https://doi.org/10.5941/MYCO.2016.44.4.338>.
- Maffioli, S.I., Sosio, M., Ebright, R.H., Donadio, S., 2019. Discovery, properties, and biosynthesis of pseudouridine, an antibacterial nucleoside-analog inhibitor of bacterial RNA polymerase. *J. Ind. Microbiol. Biotechnol.* 46, 335–343. <https://doi.org/10.1007/s10295-018-2109-2>.
- Mahmoud, H., Elsaed, W., Gabr, S., 2019. Camel Urotherapy and Hepatoprotective Effects Against Carbon Tetrachloride-induced Liver Toxicity. *Int. J. Pharmacol.* 15, 696–705. <https://doi.org/10.3923/ijp.2019.696.705>.
- McDonald, T., Drescher, K.M., Weber, A., Tracy, S., 2012. Creatinine inhibits bacterial replication. *J. Antibiot.* 65, 153–156. <https://doi.org/10.1038/ja.2011.131>.
- Minami, M., Ando, T., Hashikawa, S., Torii, K., Hasegawa, T., Israel, D.A., Ina, K., Kusugami, K., Goto, H., Ohta, M., 2004. Effect of Glycine on *Helicobacter pylori* In Vitro. *Antimicrob Agents Chemother* 48, 3782–3788. <https://doi.org/10.1128/AAC.48.10.3782-3788.2004>.
- Minato, Y., Fassio, S.R., Hase, C.C., 2013. Malonate Inhibits Virulence Gene Expression in *Vibrio cholerae*. *PLoS One* 8, e63336.
- Monod, M., 2008. Secreted proteases from dermatophytes. *Mycopathologia* 166, 285–294. <https://doi.org/10.1007/s11046-008-9105-4>.
- Mostafa, M.S., Dwedat, R.A., 2016. Antimicrobial Activity of Camel's Urine and Its Effect on Multidrug Resistant Clinical Bacterial and Fungal Isolates. *Brit. J. Pharm. Res.* 13, 29342. <https://doi.org/10.9734/BJPR/2016/29342>.
- Noor, S.O., AlAttas, S.G., Khorshid, F.K., Elsouroy, Y.A., Tawfik, N., 2015. In-Vitro Evaluation of Cytotoxicity, Antiviral and Virostatic Activity of PMF Derived from Camel Urine.
- O'hag, Mohamedani, A., 2000. O'hag & A. A. Mohamedani – Clinical trials for the treatment of ascites with camel's urine- Journal of the Arab Board of Medical Specializations Vol. 2, No. 3, July, 2000 . Journal of the Arab Board of Medical Specializations 2.
- Opperman, C.J., Copelyn, J., 2020. *Aspergillus niger* otomycosis in a child with chronic otitis externa. *S. Afr. J. Infect Dis.* 35, 128. <https://doi.org/10.4102/sajid.v35i1.128>.
- Osman, E.H., Algam, S.A., Thuwiba, M.T., Ali, M.E., Abbo, A.S., Elhassan, S.M., 2016. Antifungal effect of camel urine and ginger water extract against *Alternaria alternata* the causal agent of early blight disease of tomato in vitro. *Int. J. Agric., Forestry Plant.* 2, 261–269.
- Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., Chou, R., Glanville, J., Grimshaw, J.M., Hróbjartsson, A., Lalu, M.M., Li, T., Loder, E.W., Mayo-Wilson, E., McDonald, S., McGuinness, L.A., Stewart, L.A., Thomas, J., Tricco, A.C., Welch, V.A., Whiting, P., Moher, D., 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* n71. <https://doi.org/10.1136/bmj.n71>.
- Pai, M., Behr, M.A., Dowdy, D., Dheda, K., Divangahi, M., Boehme, C.C., Ginsberg, A., Swaminathan, S., Spigelman, M., Getahun, H., Menzies, D., Ravigliione, M., 2016. Tuberculosis. *Nat. Rev. Dis. Primers* 2, 1–23. <https://doi.org/10.1038/nrdp.2016.76>.
- Pasquetti, M., Min, A.R.M., Scacchetti, S., Dogliero, A., Peano, A., 2017. Infection by *Mycosporium canis* in Paediatric Patients: A Veterinary Perspective. *Vet. Sci.* 4, 46. <https://doi.org/10.3390/vetsci4030046>.
- Passmore, I.J., Letertre, M.P.M., Preston, M.D., Bianconi, I., Harrison, M.A., Nasher, F., Kaur, H., Hong, H.A., Baines, S.D., Cutting, S.M., Swann, J.R., Wren, B.W., Dawson, L.F., 2018. Para-cresol production by *Clostridium difficile* affects microbial diversity and membrane integrity of Gram-negative bacteria. *PLoS Pathog* 14, e1007191.
- Patel, R.V., Shah, J.S., Revathi, G., Siika, W., Shah, R., 2019. *Acinetobacter* infections: a retrospective study to determine in-hospital mortality rate and clinical factors associated with mortality. *Infect. Prevent. Pract.* 1 <https://doi.org/10.1016/j.infpip.2019.100010>.
- Pelzel-McCluskey, A., Christensen, B., Humphreys, J., Bertram, M., Keener, R., Ewing, R., Cohnstaedt, L.W., Tell, R., Peters, D.P.C., Rodriguez, L., 2021. Review of Vesicular Stomatitis in the United States with Focus on 2019 and 2020 Outbreaks. *Pathogens* 10, 993. <https://doi.org/10.3390/pathogens10080993>.
- Peng, B., Su, Y., Li, H., Han, Y., Guo, C., Tian, Y., Peng, X., 2015. Exogenous Alanine and/or Glucose plus Kanamycin Kills Antibiotic-Resistant Bacteria. *Cell Metab.* 21, 249–262. <https://doi.org/10.1016/j.cmet.2015.01.008>.
- Reyes-Jara, A., Cordero, N., Aguirre, J., Troncoso, M., Figueroa, G., 2016. Antibacterial Effect of Copper on Microorganisms Isolated from Bovine Mastitis. *Frontiers in Microbiology* 7.
- Salamat, N., Idrus, R.B.H., Kashim, M.I.A.M., Mokhtar, M.H., 2021. Anticancer, antiplatelet, gastroprotective and hepatoprotective effects of camel urine: A scoping review. *Saudi Pharm. J.* 29, 740–750. <https://doi.org/10.1016/j.jsps.2021.05.006>.
- Salwa, K., bdalla, E., Mohamed, S., Barajob, A., 2016. Novel Compounds in Lyophilized Female Camel Urine. *J. Infect. Dis. Therapy* 4. <https://doi.org/10.4172/2332-0877.1000296>.

- Schaffer, J.N., Pearson, M.M., 2015. *Proteus mirabilis* and Urinary Tract Infections. *Microbiol Spectr* 3. <https://doi.org/10.1128/microbiolspec.UTI-0017-2013>.
- Schwartz, J.H., Maas, W.K., 1960. Analysis of the inhibition of growth produced by canavanine in *Escherichia coli*. *J. Bacteriol.* 79, 794–799.
- Shinashal, R., 2014. The capability of camels urine in the treatment of infection caused by *Escherichia coli* and *Staphylococcus aureus*. *J. College Education for Pure Sci.* <http://www.iasj.net/iasj>.
- Shoeib, A., 2008. Electromicroscopic Studies of Camel Urine Effect on the Morphology of Some Human Pathogenic Bacteria, in Comparison with the Antibiotic Cefuroxime. *Saudi Journal of Biological Sciences*. *Saudi J. Biol. Sci.* 15 (3), 119–125.
- Stanojević-Nikolić, S., Dimić, G., Mojović, L., Pejin, J., Djukić-Vuković, A., Kocić-Tanackov, S., 2016. Antimicrobial Activity of Lactic Acid Against Pathogen and Spoilage Microorganisms: Antimicrobial Activity of Lactic Acid. *J. Food Process. Preserv.* 40, 990–998. <https://doi.org/10.1111/jfpp.12679>.
- Sumia, A.D., Ali, A., Majid, M.E.A., 2016. Antimicrobial activity of camels (*Camelus dromedarius*) and sheep urine on some pathogenic bacteria. *IOSR-JAVS* 9, 65–71.
- Synowiec, A., Żyła, K., Gniewosz, M., Kieliszek, M., 2021. An effect of positional isomerism of benzoic acid derivatives on antibacterial activity against *Escherichia coli*. *Open Life Sci* 16, 594–601. <https://doi.org/10.1515/biol-2021-0060>.
- Tanaka, T., Maeda, K., Fujita, K., Taniguchi, M., Oi, S., 1994. A bacteriocidal effect of 2-deoxy-d-galactose on *Escherichia Coli* due to inhibition of amino sugar metabolism. *J. Gen. Appl. Microbiol.* 40, 409–420.
- Tarr, H.L.A., 2011. The Action of Hydroxylamine on Bacteria. *J. Fisheries Board Canada*. <https://doi.org/10.1139/f53-005>.
- Tong, Z., Zheng, X., Tong, Y., Shi, Y.-C., Sun, J., 2019. Systems metabolic engineering for citric acid production by *Aspergillus niger* in the post-genomic era. *Microb. Cell Fact.* 18, 28. <https://doi.org/10.1186/s12934-019-1064-6>.
- Xu, L., Sun, X., Ma, X., 2017. Systematic review and meta-analysis of mortality of patients infected with carbapenem-resistant *Klebsiella pneumoniae*. *Ann. Clin. Microbiol. Antimicrob.* 16, 18. <https://doi.org/10.1186/s12941-017-0191-3>.
- Yadao, 2015. Review on synthesis and biological activity of derivatives of 1-(2, 4-dihydroxyphenyl)-3-phenylpropane-1, 3-dione.
- Ye, Q., Chen, W., Huang, H., Tang, Y., Wang, W., Meng, F., Wang, H., Zheng, Y., 2020. Iron and zinc ions, potent weapons against multidrug-resistant bacteria. *Appl. Microbiol. Biotechnol.* 104, 5213–5227. <https://doi.org/10.1007/s00253-020-10600-4>.
- Yehia, R.S., Osman, G.H., Assaggaf, H., Salem, R., Mohamed, M.S.M., 2020. Isolation of potential antimicrobial metabolites from endophytic fungus *Cladosporium cladosporioides* from endemic plant *Zygophyllum mandavillei*. *South Afri. J. Bot., Curre. Future Directions in Endophyte Research* 134, 296–302. <https://doi.org/10.1016/j.sajb.2020.02.033>.
- Yiase, S.G., Adejo, S.O., Gbertyo, J.A., Edeh, J., 2014. Synthesis, characterization and antimicrobial studies of salicylic acid complexes of some transition metals. *IOSR J. Appl. Chem* 7, 4–10.
- Yuan, C., Yin, Z., Wang, J., Qian, C., Wei, Y., Zhang, S., Jiang, L., Liu, B., 2019. Comparative Genomic Analysis of *Citrobacter* and Key Genes Essential for the Pathogenicity of *Citrobacter koseri*. *Front. Microbiol.* 10, 2774. <https://doi.org/10.3389/fmicb.2019.02774>.
- Żaczek, M., Weber-Dąbrowska, B., Międzybrodzki, R., Górski, A., 2020. Phage Prevalence in the Human Urinary Tract—Current Knowledge and Therapeutic Implications. *Microorganisms* 8, 1802. <https://doi.org/10.3390/microorganisms8111802>.
- Zhang, J.-L., Yao, J., Zhuge, J.-N., Zhang, Y.-J., 2019. Antibacterial activity of erythritol on periodontal pathogen. *Shanghai Kou Qiang Yi Xue* 28, 362–367.