An-Najah University Journal for Research – A
Natural Sciences

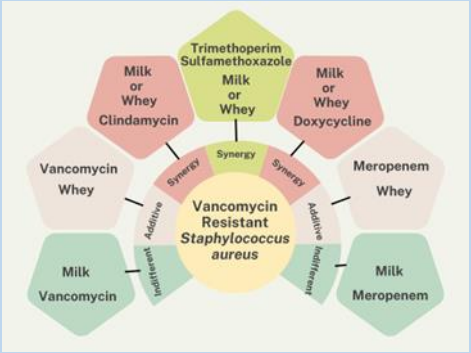
Antibacterial activity of camel milk and whey in combination with some antibiotics against vancomycin resistant *Staphylococcus aureus*

Lubna Abdallah[1,*], Ikram Sawafta[1], Nenaro Zaid[1], Rahaf Dabe[1], Mervana Mohtaseb[1], Monya Tubelleh[1] & Malak Khader[1]

Received 6th Jan. 2025, Accepted 10th Mar. 2025, Published: ××××, DOI: https://doi.org/10.xxxx

Accepted Paper, In Press

Abstract: The main goal of this research is to observe the antibacterial activity of camel milk and whey in combination with clindamycin, doxycycline, meropenem, trimethoprim sulfamethoxazole and vancomycin antibiotics against Vancomycin resistant Staphylococcus aureus (VRSA) and Staphylococcus aureus (ATCC 6538P). Micro-broth dilution method was used to measure the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) for all antibiotics, milk and whey samples. For further antibacterial investigation, the fractional inhibitory concentration (FIC) was also determined. The interpretations of the activity of camel milk and whey combined with the five examined antibiotics produced remarkable synergistic activity in most combinations against both VRSA and S. aureus. It is noticeable that camel milk showed a synergistic effect with clindamycin, doxycycline and trimethoprim sulfamethoxazole against VRSA and S. aureus. Moreover, camel whey exhibited a synergistic effect with clindamycin and doxycycline against the two isolates. Based on the obtained results, it is concluded that there was an additive or indifferent effect rather than synergism when combining camel milk and whey with antibiotics that targeted bacterial cell wall synthesis. Otherwise, when combining camel milk and whey with antibiotics targeting protein synthesis or targeting folate synthesis a synergistic effect was observed. The present research clearly showed that camel milk is considered a promising natural product that plays an important role in elevating the susceptibility of bacteria to some antibiotics.



Keywords: antibacterial activity, camel milk, camel whey, antibiotics, vancomycin resistant *Staphylococcus aureus*.

Introduction

Camel milk is an important source of nourishment since it has a number of qualities that make it a good choice for treating a variety of diseases in different parts of the world (1). It has always represented an important food source for nomadic people in arid parts of the world. Recently, camel milk has attracted great attention as a possible replacement for dairy cow's milk because of its therapeutic effects (2). Camel milk has been shown to have antibacterial, anticarcinogenic, antioxidant, anti-hypertensive, and anti-diabetic properties (3). Moreover, camel milk protection proteins may have a function in boosting the immunological defense mechanism (4). Among these proteins are whey proteins, which have anti-tumor and anti-carcinogenic properties (5). Furthermore, camel milk has significant concentrations of immunoglobulins, lactoferrin, lysozyme, and other defense proteins (6). Most of these proteins have been found to be efficient antibacterial agents. In this aspect, native or recombinant forms of camel lactoferrin have previously been shown to reduce the infectivity of the hepatitis C virus (7, 8, 9). A previous study analyzed the synergistic potential of camel lactoferrin when paired with antibiotics against methicillin-resistant *S. aureus* (MRSA) isolate in comparison to human lactoferrin. The combinations of camel lactoferrin with oxacillin or vancomycin enhanced the antibacterial activity against MRSA three times higher than human lactoferrin (10).

With the rise in multidrug-resistant infections, many patients are searching for alternatives to traditional antibiotics and antimicrobial treatments. Camel milk is at the top of the list of alternative therapies used by those patients in the Arabian and other developing regions (11-15).

Staphylococcus aureus is found in healthy people's nostrils, upper respiratory systems, and skin without causing any problems. Virulent *S. aureus* strains, on the other hand, release toxins that cause local skin degradation, fever, and severe consequences (16, 17). The emergence of methicillin-resistant *S. aureus* (MRSA) strains has complicated the treatment of staphylococcus infections because methicillin is the first line of defense against *S. aureus* infections and resistance to methicillin indicates resistance to all β-lactam medications. MRSA has become one of the most common causes of death among hospitalized patients worldwide (18-21). After MRSA outbreaks for decades, vancomycin displayed a high level of success until

1 Department of Biology and Biotechnology, Faculty of Sciences, An-Najah National University, Nablus, Palestine
* Corresponding author email: alubna @najah.edu

the first report of vancomycin-resistant *S. aureus* (VRSA) in 2002, which followed by an increased level of VRSA around the world (22). The pathogenesis and resistance patterns of *S. aureus* significantly pose a threat to human health worldwide. In the absence of effective therapeutic solutions, MRSA, VRSA and VISA (vancomycin intermediate-resistant *S. aureus*) are bacteria with the potential to cause significant mortality and destruction (23). Besides that, there are limited options for effective medications against VRSA. It is noteworthy to mention that there are several promising therapeutic options in research and development phases (24).

Our research group studied the role of camel milk and whey in combination with some common antibiotics (clindamycin, doxycycline, meropenem, trimethoprim sulfamethoxazole and vancomycin) that are usually used to treat *S. aureus* infections in order to explore and understand why camel milk can be utilized as an alternative medication for the treatment of various diseases.

Materials and Methods

Equipments

Microplate reader (Labtech, UK), sterile 96-well microtiter plates (Thermo Fisher Scientific Inc, USA). Freez-dryer (Millrock freeze dryer). Centrifuge (Sorval lynx 160)

Chemicals and reagents

Muller Hinton broth (HIMEDIA, USA), Nutrient agar (HIMEDIA, USA). Rennin (Hansens®). Antibiotics (Laboratorio, Brazil).

Milk collection and whey immunoglobulins preparation

For milk preparation, a skimmed milk sample that was previously collected by a veterinary specialist from a female camel was directly lyophilized into powder. For whey preparation, another milk sample was collected and prepared according to Brüssow et al. method (25). In order to obtain sufficient crude contraction, casein was precipitated from the pooled skimmed milk samples using rennin. The coagulated milk was then incubated at 56°C for 10 min. The casein was then separated from the lacto-serum via filtering. The lacto-serum was centrifuged once more for 30 minutes at 10,000 rpm and 4°C to make sure the whey sample was completely clear. Whey immunoglobulin pool powder was created by microfiltering the resulting supernatant and then freeze-drying it.

Antibacterial activity assay

Studied bacteria

Two bacterial isolates, *Staphylococcus aureus* (ATCC 6538P), obtained from the American Type Culture Collection (ATCC) and vancomycin resistant *Staphylococcus aureus* (VRSA) clinical isolate obtained from the Biotechnology Laboratory at An-Najah National University, were used to test the *in vitro* antibacterial activities of camel milk and whey and examined antibiotics.

Studied antibiotics

For the determination of the antibacterial profile of the two bacterial isolates, the following 19 antibiotics were used: Amikacin, Aztreonum, Cefazidime, Cefoxitin, Cefepime, Cephalothin, Chloramphenicol, Ciproflaxin, Clindamycin, Doxycycline, Erythromycin, Fusidic Acid, Gentamicin, Imipenem, Meropenem, Methicillin, Oxacillin, Trimethoprim Sulfamethoxazole and Vancomycin.

Agar disk diffusion assay

The disk diffusion method was employed to determine the antibacterial activity of the 19 antibiotics against two bacterial isolates using a standard method (26).

Micro-broth dilution assay

Minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) for camel milk, whey and the examined antibiotics (clindamycin, doxycycline, meropenem, trimethoprim sulfamethoxazole and vancomycin) were determined by the micro-broth dilution standard method (27).

Checkerboard assay

Combinations of clindamycin, doxycycline, meropenem, trimethoprim sulfamethoxazole, and vancomycin with camel milk or whey were tested against VRSA and *S. aureus* using the microdilution checkerboard technique as described by Bellio et al (28). Briefly, a final inoculum of 1×106 CFU/mL of VRSA or S. aureus was added to 96-well microtiter plates containing twofold diluted milk or whey in vertical wells and the antibiotic in horizontal wells in Muller Hinton broth. The combined antibacterial effects of milk or whey with antibiotics were diluted to reach concentrations ranging from 20 mg/mL to 0.0625 mg/mL for milk or whey, from 4 µg/mL to 0.125 µg/mL of clindamycin, from 0.5 µg/mL to 0.015625 µg/mL of doxycycline, from 2 µg/mL to 0.0625 µg/mL of meropenem, from 20/4 µg/mL to 0.625/0.125 µg/mL of trimethoprim sulfamethoxazole, and from 16 µg/mL to 0.5 µg/mL of vancomycin. These concentration ranges were chosen based on the previously obtained MIC data for each antibiotic. The fractional inhibitory concentration (FIC) was derived from the lowest concentration of antibiotic and milk or whey combination, permitting no visible growth of the test organisms on the plates. The FIC index for each agent was calculated using the following formula:

FIC (antibiotic) = MIC of antibiotic in the combination / MIC of antibiotic alone

AFIC (milk or whey) = MIC of milk or whey in the combination / MIC of milk or whey alone

Combinations were classified as synergistic, if the FIC indices were < 0.5, additive if the FIC indices were between 0.5-1, indifferent if the FIC indices were between 1 and 4 and antagonistic if the FIC indices were > 4.

Results and Discussion

The widespread use of antibiotics has led to a rise in infections in the environment and a rise in infectious microbes that are less vulnerable to the antibacterial effect. As a result of this resistance, the treatment of infections has become more challenging. Moreover, conventional antibiotic therapies have limited efficacy against infections like *S. aureus* (29). The best weapons against staphylococci are penicillin and closely related medicines from the β-lactam class. However, the widespread use of these antibiotics has resulted in a significant rise in infections that might produce β-lactamase, an enzyme that inactivate β-lactam antibiotics and causes microbial resistance (30). Therefore, there is an urgent need for novel antimicrobials to treat bacterial diseases (31). The agar disk diffusion assay revealed that the two examined bacterial isolates were multi-drug resistant, as indicated by the inhibition zone measurement.

The vancomycin resistant *S. aureus* (VRSA) isolate was susceptible only to 6 antibiotics and resistant to 13 antibiotics. while *S. aureus* (ATCC 6538P) was susceptible to 11 antibiotics and resistant to all other tested antibiotics (Table 1).

Table 1: Susceptibility testing of vancomycin resistant *S. aureus* (VRSA) and *S. aureus* (ATCC 6538P) to 19 antibiotics by the agar disk diffusion method (R; resistant, S; sensitive, I; intermediate).

Antibiotics	Vancomycin resistant *S. aureus*	*S. aureus* (ATCC 6538P)
Amikacin	S	S
Aztreonum	R	R
Cefazidim	R	R
Cefoxitin	R	R
Cefepime	R	R
Cephalothin	S	S
Chloramphenicol	S	S
Ciproflaxin	R	R
Clindamycin	S	S
Doxycycline	I	S
Erythromycin	R	R
Fusidic acid	R	R
Gentamicin	R	S
Imipenem	S	S
Meropenem	R	R
Methicilin	R	S
Oxacilin	R	I
Trimethoperim Sulfamethoxazole	R	S
Vancomycin	R	I

It is well known that certain nutritional substances can reduce the risk of human diseases. In this regard, camel milk and other functional foods are currently being utilized as an adjuvant or alternative for chemotherapy, particularly in the management and prevention of human diseases and to maintain their optimum health (32). In the current research, results demonstrated that all examined samples (the five antibiotics, camel milk and whey) are bacteriostatic agents with variation among their effective concentrations (Table 2). The resumption of bacterial growth after spreading the wells with no-growing bacteria on agar plates implied that both meropenem and vancomycin were bacteriostatic agents with no bactericidal effect. However, the others can be identified as bactericidal agents against VRSA and *S. aureus*

Table 2: Antibacterial activity of camel milk (mg/mL), whey (mg/mL) and five antibiotics (µg/mL) against vancomycin resistant *S. aureus* (VRSA) and *S. aureus* (ATCC 6538P) using micro-broth dilution assay.

	Vancomycin resistant *S. aureus*		*S. aureus* (ATCC 6538P)	
	MIC*	MBC**	MIC	MBC
Clindamycin	2±0.00	4±0.00	2±0.00	4±0.00
Doxycycline	0.06125±0.00	0.125±0.00	0.030625±0.00	0.125±0.00
Meropenem	4±0.00	-	1±0.00	-
Trimethoperim	20±0.00	40±0.00	5±0.00	40±0.00
Sulfamethoxazole	2±0.00	4±0.00	1±0.00	4±0.00
Vancomycin	16±0.00	-	16±0.00	-
Milk	5±0.00	10±0.00	5±0.00	10±0.00
Whey	10±0.00	20±0.00	20±0.00	20±0.00

Camel milk is gaining popularity as a source of human nourishment due to its unique composition and biofunctional qualities. Camel milk has a synergistic effect with some antibiotics, according to the current research findings. As the interpretations of the activity of camel milk and whey combined with the five examined antibiotics produced remarkable synergistic activity in most combinations against both VRSA and *S. aureus* (Tables 3, 4, 5 and 6). It is noticeable that camel milk and whey showed a synergistic effect with clindamycin, doxycycline and trimethoprim sulfamethoxazole against VRSA and *S. aureus*.

Table 3: Synergistic activity of the camel milk with five antibiotics against vancomycin resistant *S. aureus* (VRSA) using a checkerboard assay.

	FIC antibiotic	FIC milk	FIC index	Interpretation
Clindamycin	0.03	0.125	0.155	Synergistic
Doxycycline	0.127	0.125	0.252	Synergistic
Meropenem	0.125	1	1.125	Indifferent
Trimethoperim Sulfamethoxazole	0.06	0.125	0.185	Synergistic
Vancomycin	0.125	1	1.125	Indifferent

Table 4: Synergistic activity of the camel whey with five antibiotics against vancomycin resistant *S. aureus* (VRSA) using a checkerboard assay.

	FIC antibiotic	FIC milk	FIC index	Interpretation
Clindamycin	0.125	0.06	0.185	Synergistic
Doxycycline	0.127	0.06	0.187	Synergistic
Meropenem	0.5	0.06	0.56	Additive

Trimethoperim Sulfamethoxazole	0.25	0.125	0.375	Synergistic
Vancomycin	0.5	0.06	0.56	Additive

Table 5: Synergistic activity of the camel milk with five antibiotics against *S. aureus* (ATCC 6538P) using a checkerboard assay.

	FIC antibiotic	FIC milk	FIC index	Interpretation
Clindamycin	0.0625	0.125	0.187	Synergistic
Doxycycline	0.25	0.125	0.375	Synergistic
Meropenem	0.125	0.25	0.375	Synergistic
Trimethoperim Sulfamethoxazole	0.25	0.125	0.375	Synergistic
Vancomycin	0.0625	0.125	0.187	Synergistic

Table 6: Synergistic activity of the camel whey with five antibiotics against *S. aureus* (ATCC 6538P) using a checkerboard assay.

	FIC antibiotic	FIC milk	FIC index	Interpretation
Clindamycin	0.125	0.03	0.155	Synergistic
Doxycycline	0.254	0.03	0.284	Synergistic
Meropenem	0.5	0.06	0.56	Additive
Trimethoperim Sulfamethoxazole	0.25	0.03	0.28	Synergistic
Vancomycin	0.125	0.03	0.155	Synergistic

The antibacterial activity of camel milk and whey is in response to the availability of several protective proteins, like casein. In addition to casein, lactalbumin, and lactoglobulin, milk contains antimicrobial peptides such as lysozyme, lactoferrin, lactoperoxidase, immunoglobulins, and short peptidoglycan recognition protein (6). Lactoferrin, which is considered to be among the first lines of defense against microbial pathogens that enter the body through the mucosal tissues, as it inhibits the growth and proliferation of viruses, protozoa, fungi and bacteria, including Gram-positive and Gram-negative bacteria. A prior investigation revealed that the bacteriostatic impact of lactoferrin is owing to its capacity to bind free iron, which is one of the components required for bacterial development (33). Moreover, researchers found that there are receptors for the N-terminal region of lactoferrin on the surface of several bacteria. Lactoferrin binds to these receptors, breaking the cell wall and releasing lipopolysaccharide (LPS), which lowers permeability and makes Gram-negative bacteria more susceptible to lysozyme and other antimicrobial agents. Also, the changes in membrane permeability are caused by electrostatic interactions between the positively charged lactoferrin surface and the negatively charged lipid layer, resulting in bactericidal activity against Gram-positive bacteria (34, 35). The existence of lactoferrin in the prepared milk and whey samples in this study explains their antibacterial activity against the examined isolates (36). Radwan and his colleagues suggested that lactoferrin might stimulate cell death and growth inhibition of *S. aureus* and MRSA (10). In their experiment, vancomycin was demonstrated to cause MRSA cell membrane deterioration. The addition of camel lactoferrin provided a synergistic mode of action as MRSA membrane disorganization dramatically increased. The same observation was noticed in this research, as the combination of vancomycin with both camel milk and whey against *S. aureus* indicated a synergism. While an additive or indifferent effect of these combinations was observed against VRSA. Since the *S. aureus* isolate under investigation is vancomycin resistant. So, the addition of camel milk and whey slightly improves the vancomycin effect.

Lysozyme, the other constituent of camel milk, is a common antibacterial molecule that has a broad spectrum of antimicrobial activity. It inhibits Gram-positive bacteria and Streptococcus with muramidase activity (37, 38).

Additionally, lactoperoxidase is present in saliva, tears, and milk. It has bactericidal effects, mostly on Gram-negative bacteria, and supports the non-immune host defense system (39). Otherwise, peptidoglycan recognition protein (PGRP) stimulates the immune system's response and has robust antimicrobial activity.

Besides that, the principal protein found in milk is casein, which is present in two essential variants, A1 and A2 beta-casein. Furthermore, the main casein type in camel milk is A2 beta casein (40). Moreover, Jrad group provided that to suppress certain Gram-positive and Gram-negative bacteria, greater camel casein protein concentrations are required (41). Previous reports on caseins antimicrobial behavior noted that the native caseins provided low or no antimicrobial activity; they just released several bioactive peptides after their digestion (41, 42). Indeed, the antibacterial action of camel milk casein was raised by means of pepsin or pancreatin hydrolysis. Thus, these facts supported the research findings, as camel milk showed low bactericidal activity against the studied bacteria.

On the other hand, lactoglobulins, albumin, and immunoglobulin are among the proteins contained in whey (43). Compared to cow and buffalo milk proteins, camel whey proteins were shown to be more heat resistant. The antibacterial agents lactoferrin and immunoglobulin G are among these heat-resistant proteins (44).

Furthermore, because the whey sample under study was heated, several biofunctional peptides may have lost their activity (45). Lysozyme was thought to be the primary

component responsible for inhibitory action (46). Unfortunately, lysozyme was heat sensitive, which could explain camel whey's low activity in this study when compared to milk.

The five screened antibiotics through this running experiment affect bacteria in different mechanisms. In general, vancomycin and meropenem affect cell wall synthesis by binding with penicillin binding proteins (47, 48). While clindamycin and doxycycline inhibit protein synthesis through interaction with ribosomal subunits (49, 50). Trimethoprim/sulfamethoxazole directly affect the synthesis of folate inside microbes (51).

Conclusion

Based on the obtained results, it is concluded that there was an additive or indifferent effect rather than synergism when combining camel milk and whey with antibiotics that targeted bacterial cell wall synthesis, like vancomycin and meropenem. This is because the same mechanism may be achieved by milk constituents like lactoferrin. So, no additional value was obtained. Otherwise, when combining camel milk and whey with antibiotics targeting protein synthesis, such as clindamycin and doxycycline or targeting folate synthesis, like trimethoprim/sulfamethoxazole a synergistic effect was observed. Since milk and whey components may facilitate the entry of these antibiotics by damaging the bacterial cell wall. In addition to that, as previously mentioned, the bioactive molecules in camel milk and whey exhibit diverse mechanisms of action against bacteria.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The raw data required to reproduce these findings are available in the body and illustrations of this manuscript.

Author's contribution

Study conception and design: LA, data analysis and validation, LA, .IS, NZ, RD, MM, MT, MK; draft manuscript preparation: LA, .IS, NZ, RD, MM, MT, MK. All authors reviewed the results and approved the final version of the manuscript.

Funding

No specific fund for this research.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this article

Acknowledgements

We are grateful to the Biology and Biotechnology Department at An-Najah National University for giving us permission to use their facilities.

References

1. Attia H, Kherouatou N, Dhouib A. Dromedary milk lactic acid fermentation: microbiological and rheological characteristics. J Ind Microbiol Biotechnol. 2001; 26(5): 263-270.

2. Zhang BY, Xu S, Villalobos-Santeli JA, Huang JY. Fouling characterization of camel milk with comparison to bovine milk. J Food Eng. 2020; 285: 110085.

3. Ayoub MA, Palakkott AR, Ashraf A, Iratni R. The molecular basis of the anti-diabetic properties of camel milk. Diabetes Res Clin Pract. 2018; 146: 305-312.

4. Devendra K, Verma KA, Chatli MK, Singh R, Kumar P, Mehta N, Malav OP. Camel's milk: alternative milk for human consumption and its health benefits. Nutr Food Sci. 2016; 46:217-227.

5. Zarogoulidis P, Tsakiridis K, Karapantzou C, Lampaki S, Kioumis I, Pitsiou G, Papaiwannou A, Hohenforst-Schmidt W, Huang H, Kesisis G, Karapantzos I, Chlapoutakis S, Korantzis I, Mpakas A, Karavasilis V, Mpoukovinas I, Li Q, Zarogoulidis K. Use of proteins as biomarkers and their role in carcinogenesis. J Cancer. 2015; 6(1): 9-18.

6. Behrouz S, Saadat S, Memarzia A, Sarir H, Folkerts G, Boskabady MH. The Antioxidant, Anti-Inflammatory and Immunomodulatory Effects of Camel Milk. Front Immunol. 2022; 13:855342.

7. Redwan EM, Tabll A. Camel lactoferrin markedly inhibits hepatitis c virus genotype 4 infection of human peripheral blood leukocytes. J Immunoassay Immunochem. 2007; 28(3): 267-277.

8. El-Fakharany EM, Tabll A, Redwan EM. Potential activity of camel milk amylase and lactoferrin against hepatitis C virus infectivity in HepG2 and lymphocytes. Hepat Mon. 2008; 8: 101-109.

9. Liao Y, El-Fakkarany E, Lönnerdal B, Redwan EM. Inhibitory effects of native and recombinant full-length camel lactoferrin and its N and C lobes on hepatitis C virus infection of Huh7.5 cells. J Med Microbiol. 2012; 61(3): 375-383.

10. Redwan EM, Abd El-Baky N, Al-Hejin AM, Baeshen MN, Almehdar HA, Elsaway A, Gomaa AM, Al-Masaudi SB, Al-Fassi FA, AbuZeid I, Uversky VN. Significant antibacterial activity and synergistic effects of camel lactoferrin with antibiotics against methicillin-resistant *Staphylococcus aureus* (MRSA). Res Microbiol. 2016; 167(6): 480-491.

11. Maghraby AS, Mohamed MA, Abdel-Salam AM. Anti-schistosomal activity of colostral and mature camel milk on *Schistosoma mansoni* infected mice. Asia Pac J Clin Nutr. 2005; 14(4): 432-438.

12. Abdoun KA, Amin AS, Abdelatif AM. Milk composition of dromedary camels (Camelus dromedarius): nutritional effects and correlation to corresponding blood parameters. Pakistan J Biol Sci. 2007;10: 2724-2727.

13. Mohamad RH, Zekry ZK, Al-Mehdar HA, Salama O, El-Shaieb SE, El-Basmy AA, Al-said MGAM, Sharawy SM. Camel milk as an adjuvant therapy for the treatment of type 1 diabetes: Verification of a traditional ethnomedical practice. J Med Food. 2009; 12(2): 461-465.

14. Ehlayel MS, Hazeima KA, Al-Mesaifri F, Bener A. Camel milk: an alternative for cow's milk allergy in children. Allergy Asthma Proc. 2011; 32(3): 255-258.

15. Al-Ayadhi LY, Elamin NE. Camel milk as a potential therapy as an antioxidant in autism spectrum disorder (ASD). Evid Based Complement Alternat Med. 2013; 1-8.

16. Liu A, Garrett S, Hong W, Zhang J. *Staphylococcus aureus* Infections and Human Intestinal Microbiota. Pathogens. 2024;13(4):276.

17. Mele T, Madrenas J. TLR2 signalling: At the crossroads of commensalism, invasive infections and toxic shock syndrome by *Staphylococcus aureus*. Int J Biochem Cell Biol. 2010; 42(7): 1066-1071.

18. Klein E, Smith DL, Laxminarayan R. Hospitalizations and deaths caused by methicillin-resistant *Staphylococcus aureus*, United States, 1999–2005. Emerg Infect Dis. 2007; 13(12): 1840-1846.

19. Boucher HW, Corey GR. Epidemiology of methicillin-resistant *Staphylococcus aureus*. Clin Infect Dis. 2008; 46: S344-S349.

20. Nguyen GC, Patel H, Chong RY. Increased prevalence of and associated mortality with methicillin-resistant *Staphylococcus aureus*

among hospitalized IBD patients. Am J Gastroenterol. 2010; 105(2): 371-377.

21. Sydnor ER, Perl TM. Hospital epidemiology and infection control in acute-care settings. Clin Microbiol Rev. 2011; 24(1): 141-173.

22. Centers for Disease Control and Prevention (CDC) *Staphylococcus aureus* resistant to vancomycin--United States, MMWR. Morbidity and mortality weekly report. 2002; 51(26): 565-567.

23. World Health Organization WHO model list of essential medicines, 20th list, 2017. [Available from: https://apps.who.int/iris/handle/10665/273826].

24. Helen K, Ashlesha K. Vancomycin-resistant *Staphylococcus aureus*: Formidable threat or silence before the storm? J Infect Dis Epidemiol. 2019; 5(5).

25. Brüssow H, Hilpert H, Walther I, Sidoti J, Mietens C, Bachmann P. Bovine milk immunoglobulins for passive immunity to infantile rotavirus gastroenteritis. J Clin Microbiol.1987; 25(6): 982-986.

26. National Committee for Clinical Laboratory Standards Performance standards for antimicrobial susceptibility tests, Approved standards. NCCLS. 1999.

27. National Committee for Clinical Laboratory Standards NCCLS. Methods for Dilution antimicrobial susceptibility tests for bacteria that grow aerobically: approved standards- fifth edition. NCCLS document M7-A5. NCCLS: Wayne, PA: USA; 2000.

28. Bellio P, Fagnani L, Nazzicone L, Celenza G. New and simplified method for drug combination studies by checkerboard assay. Methods X. 2021; 8: 101543.

29. Wilson P, Andrews JA, Charlesworth R, Walesby R, Singer M, Farrell DJ, Robbins M. Linezolid resistance in clinical isolates of *Staphylococcus aureus* J Antimicrob Chemother. 2003; 51(1): 186-188.

30.Bush K, Bradford PA. β-Lactams and β-Lactamase Inhibitors: An Overview. Cold Spring Harb Perspect Med. 2016;6(8): a025247.

31. Badran I, Abdallah L, Mubarakeh R, Warad I. Effect of alkyl derivation on the chemical and antibacterial properties of newly synthesized Cu(II)-diamine complexes. Moroc J Chem. 2019; 7(1): 161-170.

32. Kris-Etherton PM, Hecker KD, Bonanome A, Coval, SM, Binkoski AE, Hilpert KF, Etherton TD. Bioactive compounds in foods: their role in the prevention of cardiovascular disease and cancer. Am J Med. 2002; 113(9): 71-88.

33. Skaar EP. The battle for iron between bacterial pathogens and their vertebrate hosts. PLoS Pathogen. 2010;6(8): e1000949.

34. Leitch EC, Willcox MDP. Synergic antistaphylococcal properties of lactoferrin and lysozyme. J Med Microbiol. 1998; 47(9): 837-842.

35. Rossi P, Giansanti F, Boffi A, Ajello M, Valenti P, Chiancone E, Antonini G. Ca 2+ binding to bovine lactoferrin enhances protein stability and influences the release of bacterial lipopolysaccharide. The International Journal of Biochemistry & Cell Biology. 2002; 80(1): 41-48.

36. Abdallah L, Sawafta A, Ben Ali S, Baradia H. Cytotoxic potential of camel whey and milk on cervix cancer (HeLa) cell line. Asian J med biol res. 2019; 5 (3):231-236.

37. Mwambete KD. The in vitro antimicrobial activity of fruit and leaf crude extracts of Momordica charantia: a Tanzania medicinal plant" Afr Health Sci. 2009; 9 (1): 34-39.

38. Narmadha G, Muneswararao K, Rajesh A, Yenugu S. Characterization of a novel lysozyme-like 4 gene in the rat," PLOS One. 2011; 6 (11): E27659–E27659.

39. Şişecioğlu M, Gülçin İ, Çankaya M, Atasever A, Özdemir H. The effects of norepinephrine on lactoperoxidase enzyme (LPO). Sci Res Essays. 2010; 5(11): 1351-1356.

40. El-Agamy EL, Nawar M, Shamsia SM, Awad S, Haenlein GFW. Are camel milk proteins convenient to the nutrition of cow milk allergic children? Small Rumin Res. 2009; 82 (1): 1-6.

41. Jrad Z, El Hatmi H, Adt I, Khorchani T, Degraeve P, Oulahal N. Antimicrobial activity of camel milk casein and its hydrolysates. Acta Alimentaria. 2015; 44(4): 609-616.

42. Pellegrini N, Colombi B, Del Rio D, Salvatore S, Bianchi M, Brighenti F, Serafini M. Total Antioxidant Capacity of Plant Foods, Beverages and oils consumed in Italy assessed by three different *in vitro* assays. J Nutr. 2003; 133(9): 2812-2819.

43. Madureira AR, Pereira CI, Gomes AMP, Pintado ME, Xavier Malcata F. Bovine whey proteins – Overview on their main biological properties. Food Res Int. 2007;40(10):1197-1211.

44. El-Agamy EI. Effect of heat treatment on camel milk proteins with respect to antimicrobial factors: a comparison with cows' and buffalo milk proteins. Food Chem. 2000; 68(2): 227-232.

45. Marks NE, Grandison AS, Lewis MJ. Use of hydrogen peroxide detection strips to determine the extent of pasteurization in whole milk. Int. J. Dairy Technol. 2001; 54(1): 20-2.

46. Nawaz N, Wen S, Wang F, Nawaz S, Raza J, Iftikhar M, Usman M. Lysozyme and Its Application as Antibacterial Agent in Food Industry. Molecules. 2022;27(19): 6305.

47. Watanakunakorn C. Mode of action and in-vitro activity of vancomycin. J Antimicrob Chemother 14 (suppl D): 1984; 7-18.

48. Cho JC, Zmarlicka MT, Shaeer KM, Pardo J. Meropenem/Vaborbactam, the first carbapenem/β-lactamase inhibitor combination. Ann Pharmacother. 2018; 52(8): 769-779.

49. Nodzo SR, Boyle KK, Frisch NB. Nationwide organism susceptibility patterns to common preoperative prophylactic antibiotics: What are we covering? J Arthroplasty. 2019; 34(7): S302-S306.

50. Patel RS, Parmar M. Doxycycline Hyclate; 2023. [Available from: https://www.ncbi.nlm.nih.gov/books/NBK555888/].

51. Kemnic TR, Coleman M. Trimethoprim Sulfamethoxazole; 2023. [Available from: https://www.ncbi.nlm.nih.gov/books/NBK513232/].