ISOLATION OF STAPHYLOCOCCUS AUREUS FROM ORAL CAVITY AND ASSESSMENT OF VANCOMYCIN-LOADED SOLID LIPID NANOPIRATES ANTIBACTERIAL ACTIVITY AGAINST MRSA

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ABSTRACT:

Staphylococcus aureus is an opportunistic that causes systemic infections and dental infections in the human being body. This organism increases its resistance to many categories of antibiotics all day and turn out to be more resistant, and this led to a growing feeling of concern in this era. Given this fact, out of (154) different oral infection samples, we were able to extract (63 (40.9%)) pure S. aureus. The prevalence of S. aureus was in Periodontal disease infection (23 (36%)), followed by Tooth decay and the frequency of S. aureus was (1524%), then Ulcerative gingivitis (10 (16%)), Dental plaque (8 (13%)), Dentin hypersensitivity (3 (5%)), While the lower incidence was 2 (3%) in Tooth impaction. The prevalence of MRSA among S. aureus were 37/63 (58.73%). The results showed MRSA high resistance to antimicrobial agents comparative to MSSA. Stimuli-responsive nano-drug delivery systems can optimize antibiotic delivery to infection sites. Nanoparticles antibacterial activity study, MIC and MBC studies of VCM-HCl, VCM-SLN, LA-SLN, AA-SLN, VCM-LA-SLN, and VCM-AA-SLN formulations against S. aureus and MRSA resistant strains are showed that S. aureus isolates was more sensitive to the prepared formulations in comparing with MRSA isolates. Among all tested formulations, the VCM-LA-SLN and VCM-AA-SLN showed significantly higher (p<0.05) antibacterial activities values against the MRSA bacteria in terms of zone of inhibition at 8 and 16 µg/ml respectively followed by VCM-SLN, then followed by VCM-HCl formulations, while AA-SLN and LA-SLN formulations showed the lowest values. Regarding MIC and MBC, they were showed the same result of antibacterial activities. MIC and MBC values of VCM-LA-SLN and VCM-AA-SLN against MRSA were about two fold more than S. aureus values. These findings suggest that VCM-loaded SLNs nanoparticles have good potential for the sustained delivery of antibiotics to dental infections. In conclusion, VCM can be effectively loaded in LNPs formulations especially VCM-LA-SLN, and VCM-AA-SLN, so these LNPs could be considered as promising delivery systems for VCM and suggest more efficient medications compared with the conventional VCM.

Keywords: Staphylococcus aureus Fromoral, Vancomycin-loaded Solid Lipid, Nanoparticles Antibacterial Activity, MRSA.

1. INTRODUCTION

The human oral cavity acts as a growth medium for pathogens as a result of its moisture, temperature, and nutritional content such as fats, carbohydrates, and protein(1). There are numerous categories of dental infections that happen in the patient's oral cavity such as periodontal disease, tooth decay, dental ache, dental plaque, dental abscess, dental calculus, dentin hypersensitivity, hyperdontia, acid erosion, malocclusion, ulcerative gingivitis, dental fluorosis, tooth impaction, acute necrotizing, etc. S. aureus is a presumed pathogen for many oral diseases, such as oral mucositis, periodontitis, peri-implantitis, endodontic infections and even dental caries(2). Drug resistant S. aureus strains are seen in a few S. aureus strains (4) developed. The strains of Staph. aureus that was resistant to antibiotics containing beta-lactams, such as Penicillins, Anoxicillin, Methicillin, Ampicillin, Cephalosporins, Oxacillin, and others (5), (6). S’. The inclination is to the right. Antibiotic resistance was acquired by aureus, resulting in a worldwide clone distribution of antimicrobial resistance expressions. Instead of MRSA strains, there are numerous bacterial diseases that cause mortality in the public and clinics (7). S. aureus
infection, like MRSA strains, has been around for a long time (7). Since the indiscriminate use of antibiotics is not a standard process, hospital facilities are not sanitary, and patients and health personnel are overburdened. Infectious bacteria, such as *S. aureus*, are spread more easily. (8) Because of its specific role in dental infections, *S. aureus* is thought to be involved (9). As a result, it makes sense to assess the state of microbial resistance to the most widely used antibiotics for treating *S. aureus*-caused dental infections. In recent decades, encapsulation of antimicrobial medicines in nanoparticle systems have emerged as a promising carrier approach for increasing therapeutic efficacy while decreasing unwanted side effects. (Troncar) Antibiotic treatment through NPS offers numerous benefits, including controlled and uniform dispersion in the target area, higher solubility, longer release, improved patient compliance, fewer side effects, and improved cellular internalization (10). It is a commercially feasible alternative to produce medications for topical, oral, pulmonary, and parenteral administration using a lipid-based drug delivery system (11). Lipid nanoparticles (LNPs) are a highly useful method for medical applications due to their important and unique properties, such as a high surface-to-mass ratio and the ability to bind and load different molecules. LNP formulations produce fine dispersion. There is absorption. The pace and method of drug release from any vehicle-mediated delivery system are essential in connection to the delivery system’s in-vivo mobility (12).

**Patients**

The study was carried out for a year, between December 2020 and November 2021. The study comprised 154 samples patients, 80 male and 76 female, ages 5 to 60, with an average age of 36.3 years. The selected cases were defined as all patients who had a major complaint of various oral infections and entered the dental clinics previously mentioned. The technique of sampling in the study was case– finding. As for determining the size of the sample, it was relied on taking all patients who attended dental clinics during the study period and estimated one year in which the study materials were collected, which included clinical and demographic data, etc. After that pus or oral swabs were collected from patients, cultivated, isolated and identified using standard laboratory methods. The oral infections include dental abscesses, periodontal abscesses, gingivitis, periodontitits, dental caries, pulpitis and oral thrush.

**Cases definition:** All patients enrolled in this study, who had a major complaint of various oral infections and entered dental clinics in the Kut city –Iraq.

**Data collection and processing:** A questionnaire was filled out for each patient with the patient’s personal and clinical data. This included age, gender, profession and relevant clinical information regarding bacterial and fungal oral infections. Upon initial hospitalization, cultures were obtained from the oral infection sites in order to isolate the causative agents of various bacteria and fungi.

**Antimicrobial Susceptibility Test**

Antibiotic resistance phenotypes (Methicillin/Oxacillin sensitivity test): All isolates of *S. aureus* were checked for the sensitivity to 1 µg Oxacillin disc and 5 µg Methicillin disc (Difco) by the disk diffusion method that instructed by NCCLS. The resistance breakpoints were ≥ 12 mm to ≤ 10 mm for 1 µg Oxacillin and ≥14 mm to ≤ 10 mm for 5 µg Methicillin. The capacity of extra antibiotic discs to inhibit MRSA or MSSA was estimated according to the instructions provided by NCCLS using commercially available discs that include: Augmenitin (AC 30 µg), tetracycline (T, 30 µg), erythromycin (E, 15 µg), ceftizoxime (CEF 20 µg), ciprofloxacin (Ci 5 µg), clindamycin (CC, 2 µg), clarithromycin (Ci 15 µg) and vancomycin (V, 30 µg). The zone of inhibition produced by *S. aureus* against each antibiotic was measured and interpreted as resistant and susceptible according to standards of Clinical Laboratory and Standards Institute15.

**Materials for Preparation of Vancomycin-loaded Solid Lipid Nanoparticles**

Sigma-Aldrich Co. Ltd. provided vancomycin hydrochloride (VCM-HCl), unsaturated FAs (linoleic acid (LA) and arachidonic acid (AA)), Solutol HS 15, and Lutrol F68 (Germany). Merck (Germany) equipped Span 80 and triethylamine (TEA), while Gattefossé equipped Compritol 888 ATO (France). Biolab Inc. (India) provided Mueller Hinton Agar (MHA) and Nutrient Broth, whereas Oxoid Ltd. provided Mueller-Hinton broth (MHB) (India).

**Preparation of SLNs**
For the preparation of SLNs, the antimicrobial actions of two of polyunsaturated fatty acids (PUFAs, free acids) and their putative mechanisms of action are described. PUFAs screening the antibacterial efficacy of unsaturated fatty acids (AA and LA) against S. aureus and MRSA was tested. Bacterial cultures were modified to 0.5 McFarland after growing overnight in Nutrient Broth at 37 °C. AA and LA submerged in dimethyl sulfoxide is serially diluted with MHB, inoculated with bacterial colonies, and then incubated in a shaking incubator at 100 rpm for 18 hours at 37 °C. To evaluate the minimum inhibitory concentration, 10 µL of each dilution were spotted on MHA plates and incubated for 18 hours at 37 °C (MIC). Triplicates of each experiment were carried out (12).

**Preparation of VCM-LA-SLNs and VCM-AA-SLNs**

Compritol 888 ATO was chosen as a solid lipid because it is used in the preparation of controlled release formulations (12). Formulations were prepared using a hot homogenization and ultrasonication method. Initial studies looked at surfactants like Solutol HS 15, Span 80, and Lutrol F68. The VCM-LA-SLNs VCM-AA-SLNs conjugates were heated to 80 °C after adding 500 mg of Compritol 888 ATO. Following melting the lipid phase, the Lutrol F68 solution (3%, w/w) was added and homogenized for 15 minutes at 6000 rpm with an Ultra Turrax T-25 homogenizer (IKA Labortechnik, Germany).

The resulting emulsion was consequently subjected to high-intensity probe sonication (30% amplitude) for 30 min at the same temperature before being cooled to 20 °C in an ice bath. The final volume of SLN dispersion was kept constant at 10 ml. The blanks, LA-SLNs and AA-SLNs, and VCM-SLNs were prepared under similar circumstances. After prepared different formulation, their physicochemical characterizations (particle size, polydispersity index-PI and zeta potential-ZP, Morphology, encapsulation efficiency (%EE) and drug loading capacity (%LC), In vitro drug release were evaluated.

**In Vitro Antibacterial Activity**

In vitro antibacterial activity VCM-HCl, VCM-SLNs, LA-SLNs, AA-SLNs, VCM-LA-SLNs, and VCM-AA-SLNs formulations against S. aureus and MRSA resistant strains were determined, the well diffusion test was carried out by using pathogenic strains (dental infection isolates collected in Wasit governorate). The bacterial suspensions with a cell density comparable to 0.5 McFarland (10⁶ CFU/mL) was transferred onto the surface of Muller-Hinton agar plates by using sterile cotton swab. Wells with 8 mm diameters prepared in the solid agar medium. Aliquots of 100 µL of each formulation concentration added into the wells (containing 16, 32, 64, 125, 250 and 500 µg/mL of VMC) for different tested formulations. The blank SLNs formulation was also used as control. After incubation for about 24 h at 37 °C, the zones of inhibition were measured (in mm) by using a caliper. Experiments were performed in triplicate (13).

**Determination of Minimum Inhibitor and Bactericidal Concentration (MIC and MBC)**

To determine MIC and MBC of VCM-HCl, VCM-SLNs, LA-SLNs, AA-SLNs, VCM-LA-SLNs, and VCM-AA-SLNs formulations against S. aureus and MRSA resistant strains, broth dilution method was used. VMC stock solutions of 500 µg/ml for different tested formulations (powders and suspensions) were prepared, and then further diluted to yield concentration range of 0.5 to 250 µg/mL (depending to their drug loading) in 4 mL of Muller–Hinton broth. Final concentration of bacteria in individual tubes adjusted to about 5x10⁸ CFU/mL by adding 50 µL of bacterial inoculum. The blank SLNs formulation was also used as control. To test MIC, after 24 h incubation at 37 °C, the test tubes were examined for possible bacterial turbidity, to detect the lowest drug concentration that could inhibit visible bacterial growth; the MBC was measured by sub-culturing from MIC broth tubes onto fresh agar plates. The in-vitro MBC value was the lowest concentration of the drug that results no growth of the bacteria that being tested (13).

**II. RESULTS AND DISCUSSION**

**Prevalence of S. aureus among various Oral Infections**

Out of (154) different oral infection samples, we were able to extract63 (40.9%) pure S. aureus. Culture, microscopic inspection, biochemical testing and APIstaph system identification kits were used to identify these isolates. Table (1) shows the prevalence of S. aureus among various oral infections. In the current study, the highest percentage of S. aureus infections was found in Periodontal disease infection 23 (36%); this bacterium can be considered one of the major agents of community- acquired S. aureus infection in Periodontal disease, followed by Tooth decay and the frequency of S. aureus was 15(24%), then Ulcerative gingivitis10 (16%), Dental plaque 8(13%), Dentin hypersensitivity 3(5%), While the lower incidence was 2 (3%) in Tooth impaction.
Table 1. Prevalence of S. aureus among various oral infections

<table>
<thead>
<tr>
<th>Oral infections type</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodontal disease</td>
<td>23</td>
<td>36</td>
</tr>
<tr>
<td>Tooth decay</td>
<td>15</td>
<td>24</td>
</tr>
<tr>
<td>Ulcerative gingivitis</td>
<td>10</td>
<td>16</td>
</tr>
<tr>
<td>Dental plaque</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>Dentin hyper sensitivity</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Tooth impaction</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>63</td>
<td>100</td>
</tr>
</tbody>
</table>

X2  47.7*  
P value 0  

*Highly significant difference (P<0.01)

The present study's findings revealed that S. aureus isolated from oral infections, which may be caused by periodontal disease, can operate as a reservoir for opportunistic microorganisms. If antibiotics are used to treat periodontal disease or other infections, they can lead to an increase in Staphylococcus spp. in the oral cavity. S. aureus strains can cause antibiotic resistance is widespread and can Periodontitis develops as a result of antibiotic therapy. The fact that S. aureus is more prevalent in the oral cavity might result in a more severe illness. The current percentages of isolated S. aureus are consistent with those reported by (14), who found that periodontal disease was 36 (33.8%), followed by tooth decay and dental plaque at 19 (26.8%) and 12 (16.9%), respectively. Also, accord with the findings of (15) who found a prevalence of S. aureus in the saliva of 21% and gingival swabs of 11% in 110 patients attending a dental hospital with a variety of oral illnesses. Salivary carriages of S. aureus was detected in 41% of patients with decreased salivary flow rates attending an oral medicine clinic, with concentrations ranging from 3.7x10^1 to 5.2x10^3 cfu/ml. Because of the variety of the normal oral flora and the healthy carriage of S. aureus in specific patient groups, the case for S. aureus in the etiology of oral dysaesthesia and mucositis is difficult. However, given the high rates of S. aureus recovery in patients with oral mucosal symptoms such as pain, burning, erythema, and swelling, physicians should consider the potential of this pathogen playing a role in oral mucosal illness.

Prevalence of Methicillin Resistant S. aureus (MRSA)

In the current study all 63 coagulase positive isolates of S. aureus were subjected to disc diffusion method to 5 μg Methicillin disc and 1 μg Oxacillin disc to determine MRSA; the test results discovered that 37 (58.73%) of isolated S. aureus were MRSA strain figure (1).

![Figure 1. Detection of (MRSA)](image)

The Susceptibility of MRSA and MSSA Isolates to Antimicrobial Agents

The Susceptibility of MRSA and MSSA isolates to antimicrobial agents where shown in the Figure (2,3). The results of current study showed the rate of MRSA was 37/63 (58.73%) from various oral infection is lower than the rate reported from Iraq in previous reports in which MRSA was isolated from 85% of health workers in Basrah city (16), also it is very lower than that reported by Hussein et al., (2015), among health care workers in Kurdistan region of Iraq, in 2015 where the MRSA prevalence was 53% On the other hand, study in Iran was 69% (17) while in a study conducted in India, the percentage was much lower 16.6% (18) MRSA prevalence.
51.4% at the Korean hospital from the Staph aureus collected from blood and nasal colonizers (19) In general MRSA was highly prevalent in Asian countries (20) In the German study there was a decrease in MRSA rate (21) In Turkey 2017, high rates of Staph aureus highly resisted to penicillin and ampicillin (22) A study in Isfahan Iran, in 2018 showed that MRSA was 51.9% among oral infection patients and 16% among health workers (23). HA-MRSA occurred at a higher rate than CA-MRSA in the world, but in Iraq the rates were similar for the HA-MRSA and CA-MRSA (19.4% and 17%, respectively), as mentioned by (12). This result can be explained by long hospitalization, random use of antibiotics, lack of awareness, and receiving antibiotics before coming to hospital, which are some of the potential predisposing factors for the appearance of MRSA in the hospital and community. Results of current study differs from that reported in the United States of America where a high incidence of MRSA occurred in a hospital-acquired S. aureus infection (HA-MRSA) (59%), compared to a community-acquired infection of S. aureus (17%) (19). This difference can be explained by the CA-MRSA biology appearing to be different from the HA-MRSA and the MSSA, which may allow CA-MRSA to cause diseases other than those expected from MSSA (24).regarding Susceptibility of MRSA and MSSA isolates to antimicrobial agents the results showed that MRSA appeared more resistant to antibiotic than MSSA. Wang also found higher antibiotic resistance rat in MRSA compared to MSSA except with Trimethoprim/Sulfamethoxazole (25) Multi-Drug Resistance (MDR) was more evident among the MRSA than MSSA (26), MRSA in this study were Multi Drug Resistant (MDR), this result was similar to previous research. (27) As this study T., Kejela and K., Bacha reported high resistance to Cifoxitin (100%) amongst MRSA isolates. highest susceptibility for Vancomycin & Gentamycin (28) MRSA is resistant to all types of antibiotics containing β -lactam (29) the resistance is conducted with low affinity for β-lactam antibiotics resulting in resistance to all β-lactams antibiotics or due enzymes that hydrolytically destroy β-lactams, MRSA may contain one or both of these mechanisms (30).

Figure 2. The Susceptibility of MRSA isolates to antimicrobial agents
Figure 3. The Susceptibility of MSSA isolates to antimicrobial agents

Prepared Formulations Properties

Hot homogenization and ultrasonication contributed to the production of smaller particle size and good properties (31). The mean particle size, PDI, ZP and morphology of prepared formulations were in nano-scale range. Adding of LA and AA improved the encapsulation of VCM in SLNs formulations. VCM-AA-SLNs and VCM-LA-SLNs achieved the best release behavior among all tested formulations within first hours followed by a constant sustained release.

In Vitro Antibacterial Activity and Determination MIC and MBC

In-vitro antibacterial activity, MIC and MBC studies of VCM-HCl, VCM-SLNs, LA-SLNs, AA-SLNs, VCM-LA-SLNs, and VCM-AA-SLNs formulations against S. aureus and MRSA resistant strains are shown in Tables 2 and Figures 3. Among all tested formulations, the VCM-LA-SLNs and VCM-AA-SLNs showed significantly higher (p<0.05) antibacterial activities values against the MRSA bacteria in terms of zone of inhibition at 8 and 16 µg/ml respectively followed by VCM-SLNs, then followed by VCM-HCl formulations, while AA-SLNs and LA-SLNs formulations showed the lowest values. Regarding MIC and MBC, they were showed the same result of antibacterial activities. MIC and MBC values of VCM-LA-SLNs and VCM-AA-SLNs against MRSA were about two fold more than S. aureus values. In general the results achieved that, by good physiochemical characterizations, increasing loading capacity, and better release behaviors for VCM-LA-SLNs and VCM-AA-SLNs, which was lead to enhance antimicrobial activity, MIC and MBC values. These findings suggest that VCM-loaded SLNs nanoparticles have good potential for the sustained delivery of antibiotics to dental infections.

Table 2. In-vitro antibacterial activity of VCM-HCl, VCM-SLNs, LA-SLNs, AA-SLNs, VCM-LA-SLNs, and VCM-AA-SLNs formulations against S. aureus and MRSA bacteria expressed as zone of inhibition (mm).

<table>
<thead>
<tr>
<th>Bacterial isolate</th>
<th>VMC conc. µg/ml</th>
<th>VCM-HCl</th>
<th>VCM-SLNs</th>
<th>LA-SLNs</th>
<th>AA-SLNs</th>
<th>VCM-LA-SLNs</th>
<th>VCM-AA-SLNs</th>
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<tbody>
<tr>
<td><strong>S. aureus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5</td>
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<td>0.0</td>
<td>NA</td>
<td>NA</td>
<td>6.7</td>
<td>4.5</td>
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<tr>
<td>1</td>
<td>NA</td>
<td>4.6</td>
<td>NA</td>
<td>NA</td>
<td>12.4</td>
<td>9.6</td>
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<td>2</td>
<td>NA</td>
<td>5.7</td>
<td>NA</td>
<td>NA</td>
<td>16.4</td>
<td>13.2</td>
<td>NA</td>
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<tr>
<td>4</td>
<td>NA</td>
<td>7.8</td>
<td>NA</td>
<td>NA</td>
<td>19.6</td>
<td>15.6</td>
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<tr>
<td>8</td>
<td>6.9</td>
<td>10.1</td>
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<td>NA</td>
<td>23.8</td>
<td>18.5</td>
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<tr>
<td>16</td>
<td>10.6</td>
<td>14.3</td>
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<td>32</td>
<td>14.6</td>
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<td>24.0</td>
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<td>7.8</td>
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<td>125</td>
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<tr>
<td><strong>MRSA</strong></td>
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<td>5.4</td>
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<td>NA</td>
<td>5.9</td>
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<td>NA</td>
<td>14.5</td>
<td>8.3</td>
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</table>
In the war against resistant bacterial infections, researchers explored the idea that the bioavailability of many antibacterial drugs was enhanced upon their incorporation within SLNs, such as clarithromycin, rifampicin, tobramycin, and ciprofloxacin (39). In vitroantibacterial activity against methicillin-susceptible and resistant S. aureus MRSA isolates.

Data are expressed as mean ± SD, n=3.

Table 3. The MIC and MBC values (µg/ml) of tested formulations VCM-HCl, VCM-SLNs, LA-SLNs, AA-SLNs, VCM-LA-SLNs, and VCM-AA-SLNs against S. aureus and MRSA isolates.

<table>
<thead>
<tr>
<th>Bacterial isolate</th>
<th>Test</th>
<th>VCM-HCl</th>
<th>VCM-SLNs</th>
<th>LA-SLNs</th>
<th>AA-SLNs</th>
<th>VCM-LA-SLNs</th>
<th>VCM-AA-SLNs</th>
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<td>S. aureus</td>
<td>MIC</td>
<td>16</td>
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<td>2</td>
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<tr>
<td></td>
<td>MBC</td>
<td>64</td>
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<td>NA</td>
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<td>4</td>
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<tr>
<td>MRSA</td>
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<tr>
<td></td>
<td>MBC</td>
<td>125</td>
<td>64</td>
<td>NA</td>
<td>NA</td>
<td>8</td>
<td>16</td>
<td>NA</td>
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</tbody>
</table>

NA= No activity.

In LA-SLNs and AA-SLNs formulations, VMC replaced with equal amount of LA and AA.

Because of the various resistance mechanisms, nanoparticulate systems may represent a promising strategy to increase drug concentration inside this strain (32). Although MRSA found to be resistant to many routinely used antibiotics; in this study it showed susceptibility to some of lading VCM formulations. It has been noted that using of nanoparticles to entrap antibacterial agents may improve their activity due to their sustained release and higher ability to penetrate the bacterial cell wall due to their small size (33). PUFAs may kill microbes by their direct action on microbial cell membranes and by increasing the formation of their bioactive metabolites that enhance the phagocytic action of leukocytes and macrophages (34).

VCM-LA-SLNs and VCM-AA-SLNs were enhanced antibacterial activity; this could be attributed to the release of VCM from the SLN over an extended period of time, as well as the combined antibacterial effect of VCM with PUFAs (LA and AA), which act by different mechanisms of action (35), thereby forming a nanoantibiotic with a dual mechanism of action against bacteria. The different mechanisms of action of VCM with LA and AA as well as the inherent ability of nanosystems to overcome microbial resistance (36) can make the development of resistance by bacteria to such a nanoantibiotic system difficult (12).

In general, the improving of antibacterial activity by VCM by SLNs was due to high lipophilicity of VCM by loading it with PUFAs-SLNs, which may have increased their penetration into the bacterial cell wall via SLNs, also the sustained release of VCM from SLNs provides enough amount through a long period of times in targeted bacteria cells. A similar enhancement in activity of an anticancer drug was observed for SLNs containing doxorubicin after co-encapsulating it with an anionic lipophilic acid (37). In our study, the demonstrated enhanced antibacterial activity of a nanoparticulate delivery system containing an antibiotic drug thus further expands the applicability of FAs in a drug delivery system (12).

SLNs are characterized by their nanosize range, thus bypassing uptake by reticulo-endothelial system; provide high protective effect of incorporated drugs from degradation, offer great targeting, and controlled release opportunity. In addition to their biocompatibility and biodegradability, the possibility of easy scale up may be another advantage (38).

In the war against resistant bacterial infections, researchers explored the idea that the bioavailability of many antibacterial drugs were enhanced upon their incorporation within SLNs, such as clarithromycin, rifampicin, tobramycin, and ciprofloxacin (39). In vitroantibacterial activity against methicillin-susceptible and resistant S. aureus MRSA isolates.
Thus, and from all above, it is reasonable to expect that the nanoparticles prepared in this study have increased inhibition zones, bacteriostatic and bactericidal effects compared with the VCM-HCl, solution alone.

III. CONCLUSION

The current study show the highest percentage of S. aureus infections was observed in Periodontal disease infection 23(36%), this bacterium can be considered the major agents of community-acquired infection. VCM was effectively loaded in LNPs and the best physicochemical properties, drug release behavior as well as antimicrobial activity were achieved by VCM-LA-SLNPs, and followed by VCM-AA-SLNPs. It seems that the hybrid delivery system of VCM-LA-SLNPs could be more promising to achieve a sustained release VCM formulation with a higher antibacterial activity.

REFERENCES

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