Review

Effectiveness of using domestic quaternary ammonium antiseptic in general medicine and dentistry (modern view and clinical case)

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Decamethoxine (DCM®) is a substance from a group of quaternary ammonium compounds. According to literary sources, the antimicrobial effect is due to a mechanism that combines damage to the cell membrane of bacteria and lysis of their protoplasts, as well as changes the permeability of the microbial cell membrane, causing its destruction. DCM® demonstrates activity against gram-positive and gram-negative bacteria (staphylococci, streptococci, diphtheria and Escherichia coli, salmonella, proteus, klebsiella, shigella, pseudomonads, clostridia), some fungi (yeast fungi, mold fungi). There are also reports of the antiviral activity of this compound. The purpose of this study was to highlight the results of the current work of Ukrainian scientists and analyze the properties and broad aspects of DCM® antiseptic, as well as demonstrate their clinical case for its effectiveness in periodontal practice. The analysis of the results of various publications allowed us to evaluate the full range of DCM® properties in terms of its therapeutic potential in modern preclinical and clinical studies, particularly in periodontal practice.

Keywords: Decamethoxine (DCM®), bactericidal action, antifungal action, antiviral action, clinical medicine, periodontology.
Introduction

Domestic antiseptic decamethoxine (DCM®), which belongs to the class of surfactants and cationic detergents, clearly stands out among the vast arsenal of modern antiseptics with antimicrobial activity. In its ability to eliminate plasmids of antibiotic-resistant microorganisms, DCM® is not inferior to miramistin and the world-famous antiseptic belonging to the derivatives of biguanidine – chlorhexidine. Experience in the treatment of diseases with a purulent-inflammatory component using DCM®, which is re-registered in Ukraine indefinitely, is accumulated in surgery, pulmonology, gynecology, urology, gastroenterology, traumatology, ophthalmology, otorhinolaryngology, dermatology and dentistry [1, 2, 3, 5, 7, 8, 14, 15, 22, 24,25, 26, 27, 29, 30, 31, 33, 38].

Materials and Methods

The methodology of the study is implemented by employing collection and analysis of evidence regarding the use of DCM® based on original and laboratory studies of domestic researchers working with evidence databases of PubMed, Scopus, Cochrane, GoogleScholar, ResearchGate and the sources of WHO, the MOH of Ukraine and other Internet resources.

Results

A significant advantage of topical antiseptics over other drugs, including antibiotics, is the slow formation of microorganism resistance that causes purulent-inflammatory and infectious diseases. The ability to increase the sensitivity of microorganisms to antibiotics is among the main positive characteristics of DCM® [4, 5, 6]. According to various information sources, the effectiveness of this drug as a local antiseptic is based on the fact that it creates a minimum risk of local side effects and tissue irritation [7, 8, 9].

Many experimental studies confirmed the high antimicrobial activity and pronounced bactericidal, bacteriostatic, fungicidal, and virucidal action of DCM®. There are two series of DCM® – generic and patented with generic preparation containing a substance identical to the original (patented) antiseptic substance. The generic DCM® preparation production technology does not fully coincide with the original patented technology; however, it does not concede to the last broad antimicrobial spectrum of action [10].

Ukrainian scientists created decamethoxine (Decamethoxinum, DCM®) at the Experimental Production of the Institute of Organic Chemistry of the National Academy of Sciences of Ukraine. Its registration certificate is UA/12128/01/01 [13]. Medicines completed with DCM® are available in Ukraine in liquid (solutions for external use, eye and ear drops), solid (tablets) forms, and with a gaseous dispersion medium in the form of an aerosol [11]. DCM® is used to treat fungal skin lesions (0.01-0.05% solution), purulent-inflammatory soft tissue injuries, inflammatory processes of mucous membranes – cystitis, otitis, conjunctivitis, gingivitis, periodontitis, stomatitis, chronic tonsillitis, sore throat, ulcerative colitis, proctitis, lung abscess, etc. (0.025-0.03% solution), as well as to treat hands and operating area (0.025% solution), suture material and tools (0.1% alcohol solution). The most common dosage form of DCM® is its 0.02% solution [12].

The structure and physical properties of DCM®

DCM® (1.10-decamethylene-bis (N, N dimethylmentoxycarbonylmethyl) ammonium chloride) is a white, fine-crystalline powder with a faint specific odor; easily soluble in water (pH of the solution is in the range of 5.5 to 7.5) and 96% alcohol. The molecular weight of the substance is 693.911 g/mol; the molecular formula is C_{38}H_{74}ClN_{4}O_{3}. A DCM® molecule contains a synthetic decamethylene chain and two molecules of menthol derived from peppermint oil [10].

The mechanism of DCM® antimicrobial action

The antimicrobial action of the compound is aimed at blocking the function of the cell wall and inhibiting the vital activity of the areas of the cell responsible for protein synthesis and cell division. DCM® action mechanism includes the destruction and increase in the permeability of the microbial wall, inactivation of exotoxin, and inhibition of protein synthesis in the bacterium cells. The specificity of the antiseptic is based on its ability to bind to lipid structures and disrupt the permeability of cell membranes, which leads to disruption of homeostasis within cells and their lysis. As a result, microorganisms’ virulence is decreased by reducing adhesiveness [14, 15]. Moreover, DCM® is selective to microorganisms and does not destroy cells in the human body. It is because the wall of a bacterial cell consists of short lipid chains, which are rapidly destroyed by DCM®, while long lipid chains of human cells are not exposed to its molecule [16].
Characteristics of antimicrobial activity of DCM® in vitro and in the experiment

DCM® has an antimicrobial effect on museum strains of microorganisms S. aureus ATCC 25923, E. coli ATCC 25922, P. aeruginosa ATCC 27853, C. albicans CCM 885, and clinical strains polyresistant to antibiotics S. aureus (n 85), E. coli (n 22), P. aeruginosa (n 16), C. albicans (n 12) with the minimum bactericidal concentration (MBCc) for S. aureus (3.67±2.71 μg/ml) and E. coli (26.8 ±17.5 μg/ml). At the same time, clinical strains of P. aeruginosa showed resistance, and C. albicans showed moderate sensitivity [17]. It was analyzed that a high MBCc characterizes DCM® in relation to 130 strains of S. aureus (1.45±0.1 μg/ml) and 120 strains of E. coli (5.99±0.37 μg/ml), in particular, Escherichia (15.6-31.2 μg/ml), Bac. subtilis (3.9 μg/ml), Bac. Anthracoid (1.95 μg/ml), clinical strains of Staphylococcus (2.19±0.23 μg/ml). In the presence of subbacteriostatic DCM® concentrations of 0.03 μg/ml and 0.1 μg/ml in the nutrient medium, the loss of the toxic effect of the exotoxin occurs in three out of five strains of diphtheria bacillus [13]. DCM® also exhibits a high bactericidal effect against clinical strains of S. aureus (n 65) – within 1.51±0.14 μg/ml, E. coli (n 55) – 4.93±0.39 μg/ml, K. pneumoniae (n 16) – 16.58±1.58 μg/ml, P. aeruginosa (n 18) – 83.33±7.15 μg/ml. The drug exhibits a fungicidal effect against C. albicans (n 10) – within 8.19±1.85 μg/ml [21]. In vitro, MBCc of the DCM® substrate depends on the type of microorganism and pH, with the lowest values for S. aureus, P. aeruginosa in an alkaline medium (pH 8.0±0.1) – 0.62 and 25.0 μg/ml, respectively [18]. At the same time, the sensitivity of Staphylococcal strains to DCM® in the presence of MBcc, which is in the range of 3.9-7.8 μg/ml, ensures the effective use of this antiseptic in clinical conditions [6], which is additionally confirmed in some studies [1, 4, 9, 10, 13, 17]. However, in the presence of 10% of blood serum proteins, MBCc DCM® increases up to 8 times, while in the presence of 5% of blood serum proteins, this concentration decreases by two times [19, 20, 21]. It was established that decamethoxine potentiates the antibacterial effect of β-lactams on resistant strains of Staphylococcus by 128 times and destroys resistance plasmids, which prevents the emergence and spread of antibiotic resistance [16].

Concentration of 0.02% DCM® solution during its long-term (for 28 days) oral administration to the gastrointestinal tract of rats at a therapeutic dose of 3 ml/kg and a dose ten times higher (30 ml/kg), the absence of pathological changes in the functioning of organs and systems of experimental animals. DCM® has been found to have no allergenic, sensitizing, local irritant properties or cumulative potential. The drug has no toxic effect on animals’ cellular and humoral immunity or reproductive function [9]. The solution of the specified concentration has a positive effect on the healing of the postoperative wound of the rabbit and the engraftment of the allograft when simulating intraperitoneal hernioplasty, minimizing the local inflammatory response and the negative impact on the processes of implanting a composite mesh into the anterior abdominal wall of animals [22].

Antiviral effect of DCM®

Mechanisms of antiviral action of DCM® are researched by studying its effect on proteolytic activity during virus-membrane interaction [23, 24, 25, 26]. It was established that DCM® has a regulatory effect on the enzymatic activity of the virus and the virus-membrane complex and inhibited proteolytic processes in the early stages of reproduction of the influenza virus during the virus interaction with membranes of sensitive cells. The mechanism of action of DCM® may be related to exposure to the extracellular virus and possible damage to the viral protease. In addition, authors suggest that the properties of this antiseptic as a surfactant are likely to interfere with the interaction between viral and cellular receptors, leading to inhibition of the proteolytic activity of the virus-membrane complex [23]. Infectious bronchitis virus (IBV) coronavirus was used as a test virus. The virucidal effect of DCM® was studied in cultures of chicken embryo fibroblast cells (FEC) and Syrian hamster kidneys (BHK21) using sterile isotonic DCM® solution at a concentration of 0.02% and 0.1%, including modern viral respiratory diseases. The results were recorded by light microscopy. It was found that the infectious titer of IBV was reduced by 2–5 lg compared to the control under conditions of treatment of the virus with saline DCM® at concentrations of 200–1000 mg/kg. It is shown that at a dose of 200 mg/kg, the tool completely inactivated 100–1000 infectious doses of the virus with an exposure duration of 30 minutes without manifestations of cytotoxic effects in serial dilutions. Revealed virucidal properties of DCM® against a prototype strain of the Coronaviridae family in pharmacologically permitted concentrations prompted the authors to recommend it as a disinfectant for non-specific prevention of coronavirus infections in adults.

According to the results of virological and clinical studies, the virucidal activity of decamethoxine in concentrations of 41.8–62.5 μg/ml (0.004–0.006% of the solution) was established in relation to amplification, which was not detected among strains resistant to the drug [24, 25]. Determining the virucidal effect of DCM® on models of simple and complex test viruses demonstrated that the 0.02% solution of DCM® proved an effective disinfectant against complex respiratory viruses, particularly the influenza virus; 0.02% solution of DCM® proved to be an effective disinfectant.
The mechanism of its virucidal action as a surfactant can be realized through the destruction of the lipid layer of the supercapsid membrane of the virus, derived from the cell membrane modified by virus-specific proteins [26].

Characteristics of DCM® properties in clinical settings (Fig. 1)

The broad spectrum of DCM® action makes it possible to use it in various fields of medicine.

**The study of the use of DCM® in the treatment of purulent wounds and burns**

The peculiarities of the wound healing process and the degree of microbial colonization of the patients' wounds in the acute period of burn disease with the topical application of means based on DCM® were monitored. The findings of the research revealed the acceleration of the reduction of wound colonization by pathogens of wound infection by microbial associations (S. aureus, A. baumannii, P. aeruginosa, etc.) starting from the 3rd day, which contributed to the reduction of the inflammatory period in the wound and eradication of these microorganisms beginning from day 7 [27].

**Study of the use of DCM® in abdominal surgery**

A comparative study of the antimicrobial effectiveness of 0.02% DCM® solution in local remediation of liver abscesses showed that bacteria of the genera Staphylococcus and Enterococcus were most sensitive to DCM®. Bacteriostatic action on Escherichia coli occurred in the presence of 8.92 mkg/ml DCM®. On the third day of DCM® use, patients were found to have enterococci and gram-negative microorganisms (Pseudomonas aeruginosa and Proteus). After seven days of treatment, in isolated cases, they had only Pseudomonas aeruginosa and Proteus vulgaris [28].

0.02% DCM® solution was used in the remediation of postnecrotic accumulations in 23 patients, of whom 82.6% achieved complete remediation of purulent foci by puncture and drainage followed by rinsing with DCM® solution. Surgical interventions (necrosequreectomy) and adequate drainage of the residual cavity were performed for 4 (17.4%) patients with tissue component (sequesters) predominating in postnecrotic clusters [29].

After surgical elimination of the source of peritonitis (local, diffuse and spilt), thorough sanitation of the abdominal cavity, removal of fibrinous-purulent plaque, exudate and washing with an antiseptic solution after installing
drainage tubes, 1.5-2 liters of warmed DCM® solution was poured into the abdominal cavity and the operating area where the wound was sutured tightly. It has been clinically proven that when using DCM®, purulent secretions from the abdominal cavity changed to serous on the 3rd day on average, which made it possible to reduce the duration of the drainage procedure [30].

**Study of the use of DCM® in otorhinolaryngology**

Today, nebulizer therapy is becoming especially popular in pharmaceutical circles. This therapy is used in the pathology of the lower respiratory tract and ENT organs. Studies have determined the effectiveness of treatment of patients with virus-induced infectious exacerbation of chronic bronchitis by inhaling antiseptic DCM® (through a nebulizer) at a dose of 2 ml of 0.02% solution 2–3 times a day for 5–7 days. The additional inhalation of DCM® was found to reduce the severity and duration of intoxication and catarhal phenomena for an average of 1–2 days [31].

The study of the clinical effectiveness of 0.02% DCM® solution inhaled as part of complex therapy of patients with infectious exacerbation of bronchial asthma allowed to establish that nebulizer therapy with DCM® solution was tolerated well by patients, was not accompanied by the development of local side effects in the form of irritation of the mucous membrane, and had a pronounced anti-inflammatory effect [32, 33].

Clinical and microbiological studies of DCM® inhalation as part of the complex treatment of infectious and respiratory complications showed the effectiveness of antiseptics in reducing the number of gram-negative microorganisms in tracheobronchial secretions after seven days of additional inhalation of DCM® compared to initial levels of microbial colonization (p <0,001) [34].

**Research on the use of DCM® in gynecological practice**

A study was conducted on the clinical efficacy of DCM® solution in preparation for surgery (extended loop excision of the cervix) in women with cervical intraepithelial neoplasia on the infection with human papillomavirus strains of high oncogenic risk in bacterial vaginosis and in the postoperative period. The findings indicate an acceleration of cervical reparative processes, pronounced antimicrobial effect, normalization of vaginal microbiocenosis, elimination of oncogenic strains of human papillomavirus and safety of vaginal use of DCM® before and after surgery [35].

**Study of the use of DCM® in dentistry**

Over the years, an extensive study of the microbiological and clinical effectiveness of DCM® use, as well as antiseptic medicines based on it, has been conducted in patients with inflammatory diseases of the oral cavity. DCM® showed high sensitivity to clinical strains of *C. albicans* in the range of 7.81–15.62 mkg/ml, bactericidal action on *S. aureus*, *S. epidermidis*, *P. aeruginosa*, *Prevotella melaninogenica* and peptostreptococci [36].

In treating chronic generalized catarrhal gingivitis, a water-based therapeutic composition (LC) was used, which included DCM® (0.1%), sodium salt of carboxymethyl starch, oxyethylcellulose and polyvinyl acetate dispersion. As a result, the high sensitivity of *E. coli* strains to LC was determined in the presence of 4.49 ± 0.27 mkg/ml. LC had a bacteriostatic effect on *S. aureus* in the presence of 0.55 ± 0.06 mkg/ml. The antifungal properties of LC were high in relation to clinical strains of *C. albicans* (minimum fungistatic concentration 8.19 ± 1.85 mkg/ml) [5]. In addition, the study was conducted on the LC’s clinical effectiveness in patients with chronic generalized periodontitis of I and II degrees of severity. Common and specialized clinical research methods proved that thanks to the method proposed by the authors, the duration of treatment of patients in the main group was reduced, and remission was prolonged compared to traditional treatment regimens [37].

Research that included the development of the composition and technology of dental films, as well as a gel based on 0.1% DCM® and chlorhexidine, showed that DCM® potentiates the effect of other antimicrobial agents in the complex therapy of dental diseases. At the same time, DCM® has a broad spectrum of antimicrobial action against gram-positive cocci (staphylococci, streptococci, pneumococci), enterobacteria, yeast-like fungi of the genus Candida, and also acts on antibiotic-resistant strains of oral Staphylococcus. It was established that during local therapy with DCM®, resistant forms of microorganisms form slowly [38].

Based on our own observations in periodontological practice, DCM® is not inferior in its properties to modern antiseptics, as demonstrated by a clinical case.
Clinical case

Examination and treatment of patient K. (20 years old) with a diagnosis of generalized periodontitis (GP) stage I (initial periodontitis) – stage II (moderate periodontitis), Grade A. Examination included checkup, history taking, X-ray examination, determination of the Silness-Loe hygiene index, periodontal indices (PMA, bleeding index), determining the depth of periodontal pockets before and after treatment. Bleeding and edema of the gums with severe hyperemia were objectively observed (Fig. 2).

Figure 2. Clinical photo of periodontal tissues of patient K., 20 years old. Diagnosis: GP stage I (initial periodontitis) – stage II (moderate periodontitis), Grade A. Condition before treatment

The X-ray revealed changes in the form of pronounced defibering of the top interdental septa with occasional damage to the integrity of the cortical plate. Indicators: hygienic index Silness-Loe – 2 points (moderate accumulation of plaque in the pockets, on the surface of the gums and teeth, visual, without probing), PMA – 2 points (inflammation of marginal gums), bleeding index – 2nd degree (the presence of numerous spotting and linear bleeding). The average depth of periodontal pockets was 3 mm.

The patient underwent professional oral hygiene according to the SRP protocol (ultrasonic scaler Woodpecker UDS-L), with elements of closed curettage of periodontal pockets, followed by rinsing with 0.02% Decasan solution (0.02% decamethoxine). Also, home rinsing of the mouth (mouth baths) with this solution was prescribed for seven days, twice a day. Immediately after treatment, the disappearance of the inflammatory process in the periodontal tissues and the presence of bleeding gums, edema and bad breath were observed. The gums became whitish-pink due to the accelerated epithelialization of tissues in the absence of irritating effects on periodontal tissues and oral mucosa. At the same time, hygienic and periodontal indices after treatment were fully normalized: hygienic index Silness-Loe – 0 points (plaque near the neck was not determined by the probe); PMA – 0 points (no gingivitis); bleeding index – 0 degrees (no bleeding). In the long-term following the treatment (after three months), the absence of redness and bleeding of the gums (Fig. 3) could be objectively stated, and the X-ray showed the stabilization of the pathological process.
Thus, we can assume that 0.02% Decasan solution is an effective drug in the local treatment of the initial manifestations of generalized periodontitis. Due to its properties, the use of Decasan helps avoid using antibiotics and nonsteroidal anti-inflammatory drugs in the periodontium’s acute course of the inflammatory process.

According to literature sources, in clinical practice, cationic polybiguanidine – chlorhexidine bigluconate – is a typical representative of surfactants in addition to DCM®. This drug also has a broad spectrum of antimicrobial action; it is included in the basic protocol for treating periodontal tissue diseases and is currently considered one of the most effective antiseptic agents in modern medicine [39, 40, 41]. Comparative characteristics of DCM® and chlorhexidine bigluconate are shown in Table 1.

**Table 1**

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<tr>
<th>Properties</th>
<th>DCM®</th>
<th>Chlorhexidine bigluconate</th>
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<tr>
<td>Bactericidal action</td>
<td>+</td>
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<td>Virucidal action</td>
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<td>Antifungal action</td>
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<td>Disinfectant action</td>
<td>+</td>
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<tr>
<td>Bacteriostatic action</td>
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<td>+</td>
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<td>Side effect</td>
<td>Minimum risk of local side effects</td>
<td>Prolonged use as an antiseptic for the oral cavity can cause temporary brown discoloration of the teeth and loss of taste sensations</td>
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<td>Effect on the respiratory system (nebulizer)</td>
<td>+</td>
<td>-</td>
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<td>Effect on the nasopharyngeal mucosa</td>
<td>+</td>
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<td>Effect of the oropharyngeal mucosa</td>
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Discussion

Summarizing the search results obtained from numerous clinical and laboratory studies, high antimicrobial and antiviral activity of DCM® antiseptic was established. It was analyzed that DCM® has an antimicrobial effect on museum and clinical strains of microorganisms S. aureus, E. coli, P. aeruginosa, C. albicans, K. pneumoniae. The sensitivity of Staphylococcal strains to DCM® in the presence of minimum bactericidal concentration, which is in the range of 3.9-7.8 μg/ml, ensures the effective use of this antiseptic in clinical conditions [6], which is additionally confirmed in some studies [1, 4, 9, 10, 13, 17]. The drug exhibits a fungicidal effect against C. albicans (n 10) – within 8.19±1.85 μg/ml [21]. It was established that decamethoxin potentiates the antibacterial effect of β-lactam resistant strains of Staphylococcus by 128 times and destroys resistance plasmids, which prevents the emergence and spread of antibiotic resistance [16]. It was determined that the concentration of 0.02% DCM® has been found to have no allergenic, sensitizing, local irritant properties or cumulative potential [9].

According to the results of virological and clinical studies, the virucidal activity of decamethoxine in concentrations of 41.8–62.5 μg/ml (0.004–0.006% of the solution) was established in relation to amplification, which was not detected among strains resistant to the drug [24, 25]. Determining the virucidal effect of DCM® on models of simple and complex testviruses demonstrated that the 0.02% solution of DCM® proved an effective disinfectant against complex respiratory viruses, particularly the influenza virus; 0.02% solution of DCM® proved to be an effective disinfectant[26].

Based on our own observations in periodontological practice, DCM® is not inferior in its properties to modern antiseptics, which is demonstrated by a clinical case. Immediatey after treatment of generalized periodontitis (stage I-II, degree A), namely after professional oral hygiene according to the SRP protocol with elements of closed curettage of periodontal pockets followed by washing them with a 0.02% Dekasan solution (0.02% decamethoxine), a decrease in the phenomena of the inflammatory process in the periodontal tissues was observed. Processes of accelerated epithelization of gum tissues were monitored against the background of the absence of an irritating effect of the drug on the mucous membranes of the oral cavity. Due to its properties, the use of Decasan helps avoid using antibiotics and nonsteroidal anti-inflammatory drugs in the periodontium’s acute course of the inflammatory process.

In conclusions: The wide spectrum of action of DCM® antiseptic (antimicrobial, antiviral, fungicidal action) and its bioavailability ensure high therapeutic efficiency not only for bacterial but also for viral infections. DCM® is not absorbed into the bloodstream through intact mucous membranes and skin and has minimum side effects. Given the proven long-term effectiveness of DCM®, it is promising to include it in new dosage forms, particularly extemporaneous drugs in periodontal practice.


Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient to publish this paper.
References


