# Emerging role of nanoemulsions in oral health management

Nanoemulsions, extensively investigated for curing many ailments, also represent a promising approach for delivering therapeutics to the oral cavity. The inherent advantages of these safe submicron drug delivery systems formulated using generally regarded as safe (GRAS) excipients approved by the Food and Drug Administration include improved bioavailability associated with a reduction of particle size, enhanced solubility, improved penetration and improved stability of the therapeutic entrapped, high loading efficiency, controlled drug release, suitability for laboratory scale and comparatively inexpensive formulation, and reduced chances of instabilities such as separation, creaming, and flocculation under the influence of gravity.[1-3] Their transparency and fluidity also enhances the esthetic appeal of the product.[4] The nanoemulsions have been reported to have broad biocidal and sporicidal efficacy against a plethora by microorganisms including bacteria, viruses, and fungi by disrupting their outer membranes.[5-8]

A number of researchers have confirmed the efficacy of nanoemulsions in prevention and treatment of diseases of the oral cavity.

Karthikeyan *et al.* formulated nanoemulsions containing soybean oil for controlling the adhesion and biofilm formation of these cariogenic bacteria on the tooth surface.[8] The authors reported a remarkable inhibitory effect on the growth of cariogenic *Streptococcus mutans* by nanoemulsions with droplets of mean diameter 308 nm. The experiments also confirmed the potential of prepared nanoemulsion in inhibiting the adherence of *S. mutans* to glass surfaces and subsequent biofilm formation. Based on the results, the authors inferred that since the nanoemulsion exhibited antiadherent effect and antibiofilm effect, they could be used as anticariogenic agents.

Lee *et al.* formulated a nanoemulsion comprising soybean oil, water, Triton X-100, and cetylpyridinium chloride. The effect of nanoemulsion on demineralization and dental caries produced on tooth blocks cut from smooth surfaces of molar teeth was studied using a continuous flow dual-organism (*S. mutans* and *Lactobacillus casei*) biofilm model and the results compared with 0.12% of chlorhexidine gluconate. The results indicated a statistically significant reduction in both the lesion depth and mineral loss after application of the cetylpyridinium chloride nanoemulsion as compared to control and 0.12% of chlorhexidine gluconate. The authors concluded that the formulated nanoemulsion had potential to cure dental caries.[9]

Fernández Campos *et al.* confirmed the enhanced antifungal activity of nystatin when administered as a nanoemulsion in treating oral candidiasis in patients suffering from mucositis.[10] In another study, Kassem *et al.* also concluded an improved antifungal activity of nystatin delivered as a self-nanoemulsifying drug delivery systems against *Candida albicans* as compared to drug suspension and marketed formulation.[11]

Li *et al.* developed a chlorhexidine acetate loaded nanoemulsion and evaluated its *in vitro* and *in vivo* antimicrobial activity against *S. mutans*. The authors concluded that the minimum inhibitory concentration and minimum bactericidal concentration of the nanoemulsion were half as compared to drug solution. Besides this, the nanoemulsion significantly reduced the number of microemulsions and severity of carious lesions in Sprague-Dawley rats.[12] Based on the observations, the authors concluded that the prepared nanoemulsion had potential for preventing and curing dental caries.

In another study, Chae *et al.* formulated a nanoemulgel gel toothpaste containing Vitamin C, E, and propolis extract and evaluated its potential in the treatment of soft-tissue wounds and ulcer-like lesions in oral cavity. The authors reported that the use of nanoemulsion-based gel in the oral cavity was effective in fast healing of the wounds with no side effects.[13]

Chae and Park reported that a nanoemulsion containing nano Vitamin C, E, and propolis exhibited anti-inflammatory, antioxidant, and antimicrobial properties and thus was could be used effectively in protection of gingiva and treatment of gingival diseases.[14]

Gavin *et al.* formulated nanoemulsions loaded with the proapoptotic drug genistein and further processed it into mucoadhesive buccal tablet formulations. The

authors reported that the prepared formulation exhibited substantial anticancer activity against oropharyngeal carcinoma. Based on the results, the authors suggested that the formulation could be a potential maintenance therapy for oral cancer patients awaiting surgical removal or postresection of identified cancerous lesions.[15]

Besides contributing to the treatment of various ailments of the oral cavity, drugs delivered as nanoemulsions are also more effective in reducing the microorganism load in equipment and water supply used for dental treatment, thereby indirectly resulting in improvement in the oral health of patients as compared to drug alone. The efficacy of a nanoemulsion containing cetylpyridinium chloride in reducing the bacterial contamination of dental chair syringe waterlines was investigated by Ramalingam *et al*.[16] The authors after exposure of the waterline biofilms to nanoemulsion for 1, 6, 12, 24, 48, and 72 h observed a significant reduction in the colony-forming units. The disinfection of the dental chair syringe waterlines by nanoemulsion in turn contributes to the improvement in oral health of patients. The mechanism by which the nanoemulsions decontaminate water is related to their kinetics, which is further attributed to high shear forces involved in their production. The shear energy is stored in oil droplets, giving them the high energy, which is passed on to bacteria upon fusion of the droplet with the bacteria, disrupting the bacterial membrane.[17]

Over the last few years, nanoemulsions for dental applications have become a potential target of patent claims as well. US patent no. US 5547677A assigned to Novavax, Inc., claimed oil in water antimicrobial nanoemulsions for oropharyngeal application as a spray or mouthwash.[7] Another patent application no. WO 2003000243 A1 filed by the Regents of the University of Michigan also claimed an antimicrobial oil in water nanoemulsion which could be either used as a toothpaste or as a mouthwash for the treatment of oral mucositis.[18] This trend of filing patents by inventors and grant of patents by regulatory authorities is increasing at a tremendous rate.

In the near future, the application of nanoemulsions is expected to increase further. Nanoemulsion-based drug delivery would be preferred by the physicians for the treatment of almost all types of oral ailments due to their site-specific local delivery in the oral cavity as well as the improved penetration of the drug into comparatively deeper layers of the oral mucosa due to the nanometric size of the nanoemulsions, thereby leading to better and complete cure of the disease. Besides this, the fact that nanoemulsions can be incorporated into other formulations such as sprays and aerosols and used in ancillary areas of dentistry like for decontamination of waterlines would also come into actual practice by physicians, which would also in turn contribute significantly to the management of oral health.

Based on the results of the above studies, it can be concluded that nanoemulsions have an excellent potential not only in prevention and treatment of oral diseases but also in reducing the microbial load in dental equipment and waterlines, thereby contributing significantly to oral health management. However, during formulation of nanoemulsions, the formulator should study the toxicity profile of surfactants, cosurfactants, and oils used in their formulation. Preference should be given to the use of GRAS category surfactants to enhance the safety of the product and in turn patient compliance. To make the formulation cost effective, a formulator should also formulate a stable and effective formulation using economical excipients.

Jasjeet Kaur Narang, Ramandeep Singh Narang[1]

Department of Pharmaceutics, Khalsa College of Pharmacy, Khalsa University, [1]Department of Oral and Maxillofacial Pathology, Sri Guru Ram Das Institute of Dental Sciences and Research, Amritsar, Punjab, India

**Address for correspondence:**
Dr. Jasjeet Kaur Narang,
Department of Pharmaceutics, Khalsa College of Pharmacy,
Khalsa University,
Amritsar, Punjab, India.
E-mail: jasjeet2975@yahoo.com

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