

## EMULGEL: IN TREATMENT OF PERIODONTITIS

Prajakta Kegade\*, Rutuja Sawant, Shreya Parkar and Akshay Gade

Department of Pharmaceutics, M Pharmacy, University of Mumbai, Vidya Nagari, Kalina, Santacruz East, Mumbai, Maharashtra 400098.

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\*Corresponding author: Prajakta Kegade

Department of Pharmaceutics, M Pharmacy, University of Mumbai, Vidya Nagari, Kalina, Santacruz East, Mumbai, Maharashtra 400098.

### ABSTRACT

Nano emulgel is the lipid based, thermodynamically stable drug delivery system. It consists of two different systems in which drug containing Nano emulsions incorporated into a gel base. The fusion of this system makes it advantageous in several ways. It is an appropriate candidate for drug delivery because of their dual character. Due to their unique property Nano-emulgel showed various applications over topically used unstable dispersions. For the enhancement of transdermal permeation, Nano-emulgel is a great approach in comparison of conventional topical formulations. It also provides controlled and sustained drug delivery and has been undertaken in achieving much better drug product effectiveness, reliability and safety. Nano-emulgel is employed as a promising approach for the treatment of periodontitis. Periodontitis is a chronic inflammatory disease affecting the supporting structure of teeth. Bacteriological studies show that periodontal diseases are infections caused by the overgrowth of Gram-negative anaerobic microorganisms. The diversity of bacterial species, the variation in composition of floras and the variation in host response to bacterial species from individual to individual are some of the major reasons that the specific aetiology of periodontal disease has not been clearly established. The plaque-induced forms of periodontal diseases are the most prevalent chronic inflammatory conditions seen in humans worldwide, affecting nearly half of the adult population. Recent studies have reported that many localized deliveries of drugs such as simvastatin, ornidazole, levofloxacin have been evaluated with positive results for periodontitis.

**KEYWORDS:** Emulgel, Gram Negative Anaerobic Microorganism, Intra Periodontal Pocket.

### 1. INTRODUCTION

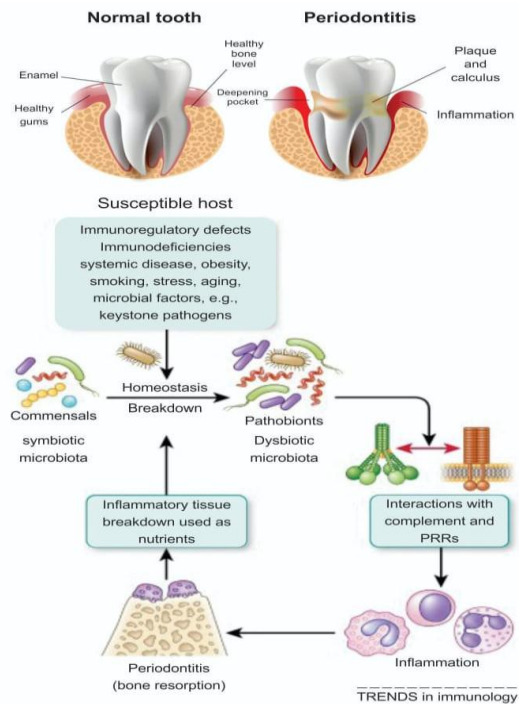
For skin disorders, the topical route is generally preferred. Topical drug delivery systems are systems in which formulation containing an active ingredient is directly applied to the skin to obtain the localizing effect of drug.<sup>[1]</sup> Emulgel is a combination of gel and emulsion where emulsion used can be of both type W/O and O/W as a vehicle for purpose to deliver selected drug to the skin. Water Phase containing the gelling agent converts a classic emulsion into emulgel.<sup>[2]</sup> Nano-emulgel, is the addition of Nano-emulsion system into gel matrix which influences a better skin permeation and residence time.<sup>[3]</sup> Nano-emulgel delivery systems have attracted attention in recent years as one of the most promising nanoparticulate drug delivery systems for topical route having a unique potential of yielding beneficial features of Nanoparticles i.e. smaller size, site specificity, high carrier capacity and that of hydrogel i.e. increase viscosity in a unit delivery system.<sup>[4]</sup> Formulation containing nano-emulsion in a gel which acts as a base is

termed as nano-emulgel. Generally emulsion has more bioavailability than emulgel but its disadvantage is less stability and poor patient compliance. Emulgel could provide benefits of both emulsion and gel.<sup>[5]</sup> The nano-emulgel for the topical delivery system acts as drug reservoirs which release drugs from the internal to the external phase and then further onto the skin. The release mechanisms depend on the composition of the polymer chains and the crosslinking density.<sup>[6]</sup> In recent years along with the topical treatment it also incorporated for the treatment of gum diseases such as periodontitis. Periodontitis is a dental inflammatory disorder affecting periodontium which is referred to the surrounding structures of the teeth. The disease is characterized by inflammation and destruction of the teeth's surrounding and supporting tissues, i.e., periodontal ligament (PDL), gum, alveolar bone which usually occur as a result of anaerobic bacterial invasion to the teeth surface and gum.<sup>[7]</sup> Nano-emulgel has several advantages over other delivery systems, including enhanced drug solubility, easily penetrate to periodontal mucosa, reduction of dose

amount, increase retention time and reduce the side effect of dose as compared to conventional formulations.<sup>[8]</sup>

### 1. Pathogenesis

Periodontitis is a chronic disease characterized by an inflammation of the periodontal tissue by the host, which is associated with dysbiotic plaque, resulting in the progressive destruction of the enamel supporting apparatus and loss of periodontal attachment.<sup>[9,10]</sup> The initial lesion begins within 2–4 days after the accumulation of the microbial plaque. During the early lesion, an acute exudative vasculitis in the plexus of the venules lateral to the junctional epithelium, movement of polymorphonuclear (PMN) cells through the junctional epithelium into the gingival sulcus, co-exudation of fluid from the sulcus, and the loss of perivascular collagen were observed. The early injury develops within 4–10 days. This injury is characterized by a dense infiltrate of T lymphocytes and other mononuclear cells, as well as by the pathological alteration of the fibroblasts.<sup>[11,12]</sup> Subsequently, the established lesion develops within 2–3 weeks. This lesion is dominated by activated plasma cells (B cells) and accompanied by further loss of the marginal gingival connective tissue matrix, but it is not detected the loss of bone. Several PMN continue to migrate through the junctional epithelium, and the gingival pocket is gradually established.<sup>[13]</sup> Finally in the advanced lesion, plasma cells continue to predominate as the architecture of the gingival tissue is disrupted, along with the destruction of the alveolar bone and periodontal ligament. Thus junctional epithelium is converted to the pocket epithelium, plasma cells and macrophages with denser inflammatory infiltrate is formed, loss of collagen attachment to the root surface, and resorption of the alveolar bone.<sup>[14]</sup> A diagrammatical comparison of healthful and diseased tooth is depicted in Fig. 1. If not properly treated, the consequence of that, along with the body's over-aggressive immune response against the microbes would lead to the destruction of the periodontium and hence loosening and loss of teeth.<sup>[15,16]</sup>



**Fig. 1: A Diagrammatic view of normal tooth and diseased tooth B Pathogenesis of Periodontal disease.**

### 2. RISK FACTOR

#### • Smoking

Smoking is one of the most important risk factors for periodontitis.<sup>[17]</sup> The smokers also present significantly increased the loss of alveolar bone and higher prevalence of tooth loss compared with non-smokers, and they have poor outcomes of all forms of periodontal treatments.<sup>[18,21]</sup>

#### • Poor oral hygiene

Poor oral hygiene is related with periodontal disease, and improper tooth brushing and oral hygiene can encourage bacterial deposition and growth of dental plaque on teeth and gums which can set a stage for inflammatory changes in periodontal tissues.<sup>[22]</sup>

#### • Hormonal changes in females

Females may experience gingival inflammation before menstruation and during ovulation due to a high level of progesterone which blocks the repair of collagen fibers and causes the dilatation of blood vessels.<sup>[23]</sup> Estrogen deficiency reduces bone density after menopause which can culminate in alveolar bone loss and eventually falling of teeth.

#### • Stress

It is clear from evidence that stress reduces the flow of salivary secretions which in turn can enhance dental plaque formation.<sup>[21]</sup> The depressed individuals have been shown to possess a higher concentration of cortisol in gingival crevicular fluid, and they respond poorly to periodontal treatment.

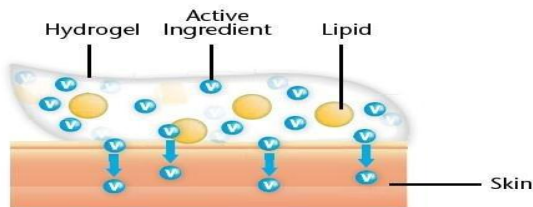
### 3. Stages of Periodontitis

**Table 1: Different Stages of Periodontitis.**

STAGES	SYMPTOMS
Acute	Receding gums Bleedings during brushing Flossing
Moderate	Pain around teeth and gum recession Inflammatory response throughout the body
Severe	Severe pain while chewing Severe Bad breath Foul taste in the mouth Loosening of teeth Alveolar Bone loss

### 4. EMULGEL

The topical delivery system is failed in the administration of hydrophobic drug. In each formulation with the active ingredients many excipients are used. To enhance the drug delivery more than one formulation can be combined; emulgel is such type of combination. It is the combination of emulsion and gel.<sup>[24]</sup> The emulsion and gel preparations have their own properties. By the use of gelling agent classical emulsion can be converted in to emulgel.<sup>[25]</sup> With respect to solid devices, semisolid (emulgel) formulations have some advantages, such as relatively faster release of the incorporated drug; easy preparation; easy to administer and a high biological compatibility and muco-adhesivity, adhesion to the mucosa in the dental pocket and fast elimination through normal catabolic pathways.



**Fig. 2: Structure of Emulgel.**

### 5. Emulgel in Treatment of Periodontitis

The current practice for the treatment of gingivitis and periodontitis involve the removal of plaque by scaling and root planning, along with application of gel directly on the gums several times.<sup>[26]</sup> In Emulgel anti-microbial, anti-bacterial, anti-inflammatory and analgesics drugs are incorporated. Anti-microbial property of the Chlorhexidine, a biguanide compound, has been shown to possess a broad-spectrum of topical activity.<sup>[27]</sup> It has been used by dental professionals for plaque control and for the treatment of gingival inflammation.<sup>[28]</sup> Chlorhexidine was primarily used in mouth-rinses and was suggested in the hygiene phase of treatment as an adjunct to tooth-brushing. Most attention, however, has been focused on the use of chlorhexidine during the operative and immediate post-operative phases of non-surgical and surgical periodontal treatment.<sup>[29]</sup>

### 6. Components

For the preparation of emulgel some constituents used are:

#### Aqueous Material

Commonly used agents are water, alcohols<sup>[30]</sup> Vehicle should have following ideal properties

- Deposition of the drug on the skin with even distribution.
- Release the drug so it can reach to the site of action.
- The drug is delivered to the target site
- To provide a pharmacological effect in the targeted tissue for sufficient duration.
- Depending on characteristics, rate and extent of absorption vary.<sup>[31]</sup>

#### Oil

Oils are used for preparation of emulsion. Mineral oils and paraffin are used either alone or in combination.<sup>[32]</sup> These agents form the oily phase. soft or hard paraffin combined with externally applied emulsions, mineral oils, are broadly used both as the vehicle for the drug and for their occlusive and sensory characteristics. Oils are used in oral preparations are non-biodegradable mineral and castor oils that provide a local laxative effect, and fish liver oils or numerous fixed oils of vegetable origin (e. g., Arachis, cottonseed, and maize oils) as nutritional supplements.<sup>[31,33]</sup>

#### Emulsifiers

Emulsifiers used for preparation of emulsion. Some examples are span 80, tween 80, stearic acid, sodium stearate. To control stability and to promote emulsification during manufacture emulsifying agents are used. e.g. polyethylene glycol 40 stearate,<sup>[34]</sup> sorbitan monooleate (span 80),<sup>[35]</sup> polyoxyethylenesorbitan monooleate (tween 80),<sup>[36]</sup> stearic acid,<sup>[37]</sup> sodium stearate.<sup>[36]</sup>

#### Gelling agents

Gelling agents are used for prepare gels, which enhance consistency of any dosage form can also be used as thickening agent. Carbopol-940 1% HPMC-2910.<sup>[38]</sup>

#### Penetration enhancers

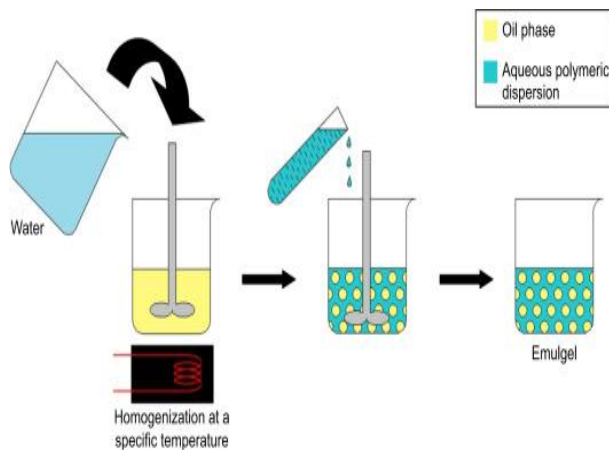
Penetration enhancers help to absorb drug to the skin. These are agents used to interact with skin and partition into, to induce a temporary and reversible increase in skin permeability.<sup>[33]</sup> Vehicles often include penetration enhancing ingredients, to promote absorption of drugs. That disrupts the skin barrier, fluidize the lipid channels, to enhance delivery into skin. E.g. Clove oil 8%, Menthol 5%.<sup>[39]</sup>

### 7. Method of Preparation

STEP1: Formulation of Emulsion either O/W or W/O

STEP2: Formulation of gel base

STEP3: Emulsion is incorporated into gel base with continuous stirring.<sup>[40,41]</sup>



**Fig. 3: Preparation of Emulgel.**

Emulgel are prepared by incorporating gel and emulsion separately. Emulsion is prepared by, aqueous phase and oil phase separately and then mixed together. Then the gel is prepared by using gelling agent. After preparing gel and emulsion, they are mixed together with gentle stirring. The chemicals are used as oil phase are castor oil, clove oil, liquid paraffin, etc. Water and alcohol are used as aqueous phase.<sup>[42]</sup> The aqueous phase is prepared by mixing tween 80 and water and also the oil phase prepared by mixing paraben and propylene glycol. The drug is dissolved in ethanol and the two phases are mixed with continuous stirring. Then the polymers are dissolved in water with the pH of 6.0-6.5.

## 8. Advantages

- Avoid first pass metabolism.
- Avoid gastrointestinal incompatibility.
- Selective for a specific site.
- Improve patient compliance.
- Suitable for self-medication.
- Better loading capacity
- Better stability
- No intensive sonication<sup>[33,43,44]</sup>

## 9. Evaluation

### • Clarity

The clarity is determined by visual inspection under black and white background.

### • Gel-Strength

The Strength can be evaluated using a rheometer. Depending on the mechanism, a specified amount of gel is prepared in a beaker, from the sol form. The gel containing beaker is raised at a certain rate, so pushing a probe slowly through the gel. The adjustments in the load on the probe may be measured as a function of intensity of immersion of the probe beneath the gel floor.<sup>[45]</sup>

### • Physical examination

Emulgel were inspected for their visual appearance, homogeneity, consistency, grittiness and phase separation.<sup>[46]</sup>

### • Drug content measurement

Drug content is measured using UV spectrophotometer. Take 1gm of emulgel. Mix in solvent in order to obtain clear solution. Absorbance is determined using UV spectrophotometer.<sup>[47]</sup>

### • Spreadability

Spreadability is suggested by Mutimer *et al.* (1956) which is modified in the laboratory and used for the study. It is measured on the basis of "Slip" and "Drag" characteristics of emulgel.<sup>[32]</sup> A shorter interval indicates better spreadability.<sup>[48]</sup>

### • Rheological study

The viscosity of the batches was determined using a cone and plate viscometer with spindle 7 (Brookfield Engineering Laboratories). The assembly was connected to a thermostatically controlled circulating water bath maintained at 25°C. The formulation whose viscosity was to be determined was added to a beaker covered with thermostatic jacket. Spindle move into the emulgel and the reading was noted.<sup>[42]</sup>

### • Globule size and its distribution

Globule size and distribution are determined by Malvern Zeta size. A 1.0 g sample is dissolved in purified water and agitated to get homogeneous dispersion. The sample was injected to photocell of Zeta size. Mean globule diameter and distribution are obtained.<sup>[36,49]</sup>

### • Stability studies

The Emulgel were packed in aluminium collapsible tubes and subjected to studies at 5° C, 25° C/ 60%, and 40° C/75% RH for a period of 3 months. Samples were taken at 15-day time intervals and evaluation for physical appearance, pH, rheological properties, drug content, and drug release profiles is done.<sup>[50]</sup>

### • Swelling index

The swelling index of emulgel is determined by taking 1 g of gel on porous aluminium foil and then placed in a 50 ml beaker containing 10 ml 0.1 N NaOH separately. These samples are removed from beakers at different time intervals and put it on a dry place for some time after it reweighed. Swelling index is calculated as follows:

$$\text{Swelling index (SW) \%} = [(Wt - Wo)/Wo] \times 100$$

Where, (SW) % = Equilibrium percent swelling, Wt = Weight of swollen Emulgel after t(time), Wo = Original weight at zero time.<sup>[24,51]</sup>

### • Skin irritation test (Patch Test)<sup>[30]</sup>

The prepared emulgel is applied on the skin of rat. Change in colour, change in skin morphology is checked up to 24 hours. The total set of 8 rats can be used of the study. If no irritation occurs the test is passed. If the skin irritation symptom occurs in more than 2 rats the study should be repeated.<sup>[50]</sup>



## 10. Marketed Preparation

Marketed preparation are listed in table 2.<sup>[52]</sup>

**Table 2: A Summaries of drug used in the preparation.**

Polymer	Drug	Inferences
Poly-gamma-glutamic acid (In situ)	Metronidazole	Nontoxic photoactive hydrogel with significant swelling ratio for treatment of periodontal disease
Gellan gum, Lutrol	Ornidazole	Smart gel periodontal drug delivery system offered a numerous physical and drug release features
Chitosan	Simvastatin	Improvement in conditions like modified sulcus BI, PD, clinical attachment level and bone fill
Pluronic	Moxifloxacin	Safe gel showing particular inhibition of <i>P. gingivalis</i> and decline in PD

## CONCLUSION

The new concept of formulation emulsion in gel has shown better delivery of the drug and emulsion is better stabilize in the gel. The recent developments in nanomaterials and nanotechnology have provided promising opportunities for the effective management of periodontitis. From these novel technique, biologically adhesive polymers are used to achieve extended drug release, the increase of intra-pocket drug penetration, the enhancement of mechanical properties, and the possibility of loading multiple drugs in a unit delivery system have better result. Furthermore, the advent of smart-nano-emulgel innovations whereby drug release may be control by stimuli responses gives additional promising opportunities in achieving optimum therapeutic effect. The future utilization of these advantages will significantly improve dental care as provide the controlled release effect, that improves the bioavailability of that drugs.

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