FORMULATION AND EVALUATION OF TWO LORATADINE GEL EMULSIONS

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Abstract: Emulgels represent a promising topical drug delivery system that combines the advantages of emulsions and gels, offering improved stability and patient acceptability. Loratadine, a second-generation antihistamine with poor aqueous solubility, may benefit from incorporation into an emulgel system for topical application. The aim of this study was to compare two loratadine-loaded emulgel formulations differing only the type of surfactant used: sodium lauryl sulfate (SLS) and Tween 20. Both formulations were prepared under identical conditions and evaluated with respect to emulsion stability and consistency of the final emulgel. The formulation containing SLS exhibited reduced emulsion stability and resulted in an emulgel with lower consistency and more fluid behavior after incorporation into the gel base. In contrast, the formulation containing Tween 20 showed improved emulsion stability and produced more homogeneous emulgel with higher consistency. These differences are attributed to the influence of surfactant type on emulsion stability and its interaction with carbomer-based gel network. The findings suggest that non-ionic surfactants such as Tween 20 are more suitable for the development of stabile loratadine emulgel formulations.
Keywords: emulgel, loratadine, topical drug delivery, semi-solid dosage forms, gels, emulsions

1. INTRODUCTION

Topical drug delivery systems have gained increasing interest due to their ability to deliver active pharmaceutical ingredients directly to the site of action while minimizing systemic exposure and associated adverse effects (Ansel, Allen, & Popovich, 2021; Benson & Watkinson, 2012). Among various topical dosage forms, emulgels have emerged as a promising delivery platform by combining the advantages of emulsions and gels, resulting in improved physical stability, ease of application, and enhanced patient acceptability (Aulton & Taylor, 2022; Patel, Patel, & Patel, 2011; Mohamed, 2004).

Loratadine is a second-generation H_1-antihistamine widely used in the treatment of allergic conditions. It is characterized by low aqueous solubility and high lipophilicity, classifying it as a Biopharmaceutics Classification System (BCS) class II drug (Sinko, 2016; Katzung, Trevor, & Kruidering-Hall, 2021; Waller, Sampson, & Renwick, 2015). Although loratadine is conventionally administered orally, this route may be associated with limited bioavailability and adverse effects such as headache, fatigue, and gastrointestinal disturbances (Sweetman, 2011). Consequently, topical formulations of loratadine have been investigated as an alternative approach for the treatment of localized allergic skin conditions, provided that an appropriate carrier system is employed (Bhowmik, Chiranjib, & Jayakar, 2012).

The formulation of emulgels requires careful selection of excipients, particularly surfactants, which play a crucial role in reducing interfacial tension, facilitating emulsion formation, and influencing droplet size, physical stability, and rheological properties of the formulations (Aulton & Taylor, 2022; Florence & Attwood, 2016). Furthermore, interactions between surfactants and gel-forming polymers may alter the internal structure of the gel network, thereby affecting consistency and mechanical properties of the final emulgel (Tadros, 2013).

Ionic surfactants, such as sodium lauryl sulfate (SLS), exhibit strong surface activity but may negatively influence formulation stability and viscosity due to electrostatic interactions with polymeric gel networks (Aulton & Taylor, 2022). In addition, SLS has been associated with an increased potential for skin irritation when used in topical formulations (Rowe, Sheskey, & Quinn, 2019). In contrast, non-ionic surfactants such as Tween 20 (polysobates) are widely used in dermatological formulations owing to their good compatibility with a wide range of excipients, lower irritation potential, and favorable stabilizing properties in oil-in-water emulsions (Rowe et al., 2019).

Despite the extensive applications of emulgels in topical drug delivery, comparative studies evaluating the influence of surfactant type on emulsion stability and emulgel consistency remain limited (Khan, Ahmad, & Raza, 2024; Ghosh, Ghosh, & Reddy, 2021). Therefore, the present study aimed to compare two loratadine-loaded emulgel formulations prepared using different surfactants - SLS and Tween 20, under identical formulation and processing conditions, with particular emphasis on emulsion stability and emulgel consistency.

2. MATERIALS AND METODS

Materials

Loratadine (micronized, pharmacopoeial grade) kindly donated by ReplekAD (Skopje, North Macedonia), sodium lauryl sulfate (Carl ROTH), Tween 20 (Merck), paraffinum liquidum (Interhem, Skopje), propylene glycol (Interhem Skopje), methyl paraben (Interhem Skopje), ethanol (Alkaloid, Skopje), Carbopol (Interhem, Skopje), triethanolamine, and distilled water were used for the preparation of emulgel formulations.

Two loratadine emulgel formulations were prepared, differing only in the surfactant used:

- **Formulation 1 (F1**): Emulgel containing SLS;
- **Formulation 2 (F2):** Emulgel containing Tween 20.

All other components and their concentrations were kept constant to enable direct comparison of the effect of surfactant type.

3. PREPARATION OF GEL BASE

The gel base was prepared using Carbopol as the gelling agent. Carbopol was dispersed in distilled water under continuous stirring until complete hydration was achieved. Triethanolamine was then added dropwise to neutralize the dispersion and initiate gel formation, resulting in a clear and homogenous gel base. The gel was allowed to equilibrate to ensure complete polymer swelling prior to incorporation of the emulsion.

4. PREPARATION OF EMULSION PHASE

Loratadine was dissolved in ethanol to obtain a clear drug solution. Methyl paraben was dissolved separately in propylene glycol. The two solutions were mixed and incorporated into the aqueous phase containing distilled water. Parafinum liquidum constituted the oil phase. Both, aqueous phase and the oil phase were heated separately to 65° C in a water bath. The oil phase was gradually added to the aqueous phase under continuous stirring to form an oil-in-water emulsion. Stirring was continued until a uniform emulsion was obtained which was then allowed to cool to room temperature.

5. PREPARATION OF EMULGEL

The cooled emulsion was incorporated into the Carbopol gel base in a 1:1 ratio under gentle stirring to obtain the final emulgel. Care was taken to ensure uniform mixing and to avoid air entrapment. The resulting emugels were evaluated visually for homogeneity and consistency.

6. EVALUATION OF EMULSIONS AND EMULGELS

The prepared emulsions and emulgels were evaluated visually for physical stability, homogeneity and consistency (European Pharmacopoeia, 2023). Visual inspection was performed immediately after preparation and during storage at room temperature. The evaluation focused on the presence of phase separation, creaming, changes in appearance, and differences in consistency between the two formulations.

7. RESULTS AND DISCUSSION

Visual evaluation of the emulsions prior to incorporation into the gel base revealed noticeable differences in physical stability. The emulsion prepared with SLS (F1) exhibited reduced stability, characterized by faster onset of creaming and decreased homogeneity upon standing. In contrast, the emulsion prepared with Tween 20 (F2) remained visually stable for longer period, showing improved homogeneity and no immediate signs of phase separation.

After incorporation of the emulsions into the Carbopol gel base at a 1:1 ratio, clear differences in the consistency of the final emulgels were observed. The emulgel containing SLS (F1) demonstrated lower apparent viscosity and more fluid behavior, suggesting partial disruption of the carbomer gel network, possibly due to electrostatic interactions between the ionic surfactant and the polymer. Conversely, the emulgel containing Tween 20 (F2) exhibited higher consistency, better homogeneity and improved structural integrity of the gel matrix. These findings are consistent with the literature reports indicating that non-ionic surfactants are generally more compatible with carbomer-based gel systems (Aulton & Taylor, 2022).

8. CONCLUSION

Two loratadine-loaded emulgel formulations were successfully prepared under identical formulation and processing conditions, differing only in the type of surfactant employed. The formulation containing sodium lauryl sulfate exhibited lower emulsion stability and produced an emulgel with lower consistency and increased fluidity. In

contrast the formulation containing Tween 20 demonstrated improved emulsion stability, enhanced homogeneity, and higher consistency of the final emulgel.

The results highlight the significant influence of the surfactant type on emulsions behavior and its interaction with carbomer-based gel network. Non-ionic surfactants such as Tween 20 are more suitable for the development of stable loratadine emulgel formulations. These findings emphasize the importance of the rational excipient selection in emulgel formulation design and provide a basis for further optimization and evaluation of topical loratadine delivery systems.

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