Formulation and Evaluation of Thermostable Gel for Acne treatment using Clindamycin

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Abstract

The medium for formulation of a gel is selected according to its desired application. The medium could be one or more solvents depending upon the use of the gel. Methodology: Formulation of Clindamycin-ZAD topical thermostable gel for Acne treatment: Hydrogel is a network of polymer chains that are hydrophilic, sometimes found as a colloidal gel in which water is the dispersion medium. Hydrogels are highly absorbent (they can contain over 99% water) natural or synthetic polymers. Result and Discussion: As a result of these experiments, we have arrived at a final formula for the topical application of gel to be used in Acne Vulgaris containing Clindamycin Phosphate.

Key-words: Gel, Acne, Clindamycin

Introduction

Acne vulgaris is one of the commonest skin disorders which dermatologists have to treat. It mainly affects adolescents, though it may be present at any age. Acne by definition is multifactorial chronic inflammatory disease of pilosebaceous units. Various clinical presentations include seborrhoea, comedones, erythematous papules and pustules, less frequently nodules, deep pustules or pseudocysts, and ultimate scarring in few of them. Acne has four main pathogenetic mechanism—increased sebum productions, follicular hyper keratinization, Propionibacterium acne (P. acne) colonization, and the products of inflammation. In recent years, due to better understanding of the pathogenesis of acne, new therapeutic modalities are being designed. Availability of new treatment options to complement the existing armamentarium should help to achieve the successful therapy of greater numbers of acne patients, ensure improved tolerability and fulfil patient expectations. Successful management of acne needs careful selection of anti-acne agents according to clinical presentation and individual patient needs. Gelsare semisolid preparations intended for application on the skin or the accessible mucous membranes like oral cavity.

A gel is formed by creating a balance between the polymer and the solvent. A critical concentration yields the gel, also known as the gelling point, below this point the gel cannot be formed while above this point the viscosity increases greatly. The gelling point can be determined using the hydrophilic and lipophilic balance of the polymer, solvent and polymer interaction, uniformity in the structure, molecular weight of the polymer and flexibility of the polymer chain.

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Many polymers, including natural ones like xanthan gum, starch, gellan, konjac, carrageenan, collagen, fibrin, silk fibroin, hyaluronic acid and gelatin, form gels by several main mechanisms as discussed by Gasperini. These are often usefully temperature sensitive in terms of viscosity change, but thermoresponsive design will increasingly be combined with synthetic features that relate to specific monomeric inclusion that may transduce to a thermal signal or act independently. However, innovative types are also often thermally responsive in terms of outputs other than viscosity or volume, examples being opacity, colour (thermochromic), hydrophobicity and electroconductive.

**Clindamycin phosphate**
Clindamycin is a lincosamide antibiotic with primarily bacteriostatic action against Gram positive aerobes and wide range of anaerobic bacteria.

![Clindamycin Structure](image)

**Pharmacokinetics**
Food does not interfere with absorption of clindamycin. Only ~10% clindamycin is excreted unchanged in the urine, and small quantities are found in the faeces. Though, antimicrobial activity continues in faeces for 5 days after parenteral therapy with clindamycin is stopped; growth of clindamycin-sensitive microorganisms in colonic substances may be inhibited for up to 2 weeks.

**Material and Methods**
**Materials used in preparation of Thermostable Gel for Acne treatment**
- Clindamycin phosphate (CP) [Sarvasya Trading Pvt. Ltd, Surat]
- Zinc acetate dihydrate (ZAD)
- Ethanol
- Propylene glycol
- Carbopol 940
- Hydroxypropyl cellulose
- Sodium carboxymethyl cellulose (Na-CMC)
- Hydroxyethyl cellulose
- Guar-gum
- Sodium hydroxide (NaOH).

**Evaluation of thermostable gel**

**Physical appearance:** The physical appearance and homogeneity of the prepared gels were tested by visual observations.

**Spread ability test:** Spread ability can be determined by applying the gel over an even surface and observed for the gritty nature of the hydrogel if present.

**Results and Discussion**
**Characterization of Pure Drug (Clindamycin Phosphate)**

<table>
<thead>
<tr>
<th>Test</th>
<th>Specification</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>White</td>
<td>Confirms</td>
</tr>
<tr>
<td>Physical State</td>
<td>Crystalline Powder</td>
<td>Confirms</td>
</tr>
<tr>
<td>Identification</td>
<td>Melting point – 208°C to 211°C</td>
<td>209°C</td>
</tr>
<tr>
<td>pH of 10% water solution</td>
<td>3.5 to 4.5</td>
<td>3.9</td>
</tr>
</tbody>
</table>

**Selection of gelling agent for formulation**
- Trial baths with different gelling agents were formulated and were initially visually observed for their appearance and viscosity. Their consistency/viscosity were checked. Consistency/viscosity of formulations prepared using Hydroxyethyl cellulose was found superior to other gelling agents and physical appearance was also better. Hence, it was selected for further analysis and optimization.

**Effect of different concentration of zinc acetate dihydrate on complex formation**
- To formulate a stable CP-ZAD Complex concentration of ZAD was varied and its effect on viscosity of complex was observed.

**Conclusion**
Based on the various studies carried out in the formulation trials, we arrived to the following conclusions: Zinc acetate dihydrate forms stable complex with Clindamycin.
Phosphate at pH 7.5 pH and Viscosity were found to be satisfactory. API Content (Assay) and RS at stability conditions were found to be within range as per US Pharmacopoeia.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Zinc acetate dehydrate 10% w/w solution (100 mg/ml)</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100 mg</td>
<td>Less viscous complex</td>
</tr>
<tr>
<td>2</td>
<td>200 mg</td>
<td>Less viscous complex</td>
</tr>
<tr>
<td>3</td>
<td>300 mg</td>
<td>Less viscous complex</td>
</tr>
<tr>
<td>4</td>
<td>400 mg</td>
<td>Moderately viscous complex</td>
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<tr>
<td>5</td>
<td>500 mg</td>
<td>Complete viscous complex</td>
</tr>
<tr>
<td>6</td>
<td>600 mg</td>
<td>More viscous complex</td>
</tr>
<tr>
<td>7</td>
<td>700 mg</td>
<td>Highly viscous complex</td>
</tr>
</tbody>
</table>

Effect of concentration of ZAD on Viscosity of Complex.

References

5. Mistry A, Ravikumar P. Development and evaluation of azelaic acid based
12. Webster GF, Guenther L, Poulin YP, et al. A multicenter, double-blind, randomized comparison study of the efficacy and tolerability of once daily tazarotene 0.1% gel and adapalene 0.1% gel for the treatment of facial acne vulgaris. Cutis 2002;69 (Suppl):