

# Formulation Design and Evaluation of Hydrocortisone Gel for Topical Use

Wisam A. Hussein<sup>1</sup>, Suhad T. Zamil<sup>2\*</sup>, Suaad T. Zamil<sup>3</sup>, Muhammed A. Hussain<sup>4</sup>, Hussein A. Kadhim<sup>4</sup>

<sup>1</sup>Department of Surgery, College of Medicine, University of Kufa, Kufa, Iraq

<sup>2,3</sup>Department of Pharmacology and Toxicology, College of Pharmacy, University of Kufa, Kufa, Iraq

<sup>4</sup>Department of Pharmacology and Therapeutics, College of Medicine, University of Kufa, Kufa, Iraq

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## ABSTRACT

Hydrocortisone is a corticosteroid drug used for topical atopic dermatitis treatment available in the form of a spray, rectal cream, powder for preparation and injection, ointment in concentrations: 0.5, 1, 2.5%, ear solution 1%, topical solution in concentrations: 0.1, 2.5%, rectal suppositories, suspension solution plus tablets.

Hydrocortisone gel was manufactured and evaluated *in-vitro* model by examining the physical and chemical properties, as well as evaluating the rheological properties with a texture analyzer, also evaluated. The stability of accelerated hydrocortisone gel, thermal, chemical and acid stability of the components were also evaluated. The feasibility study was also completed. All of these evaluations were compared relative to the commercial formulas and statistical analyzes were conducted.

The results of hydrocortisone gel compared to the commercial formula showed optimum physicochemical properties, good rheological properties, and good stability. From the general results, we can conclude that hydrocortisone gel is a practical, more effective, safe and stable formulation when compared to its counterparts.

**Keywords:** Corticosteroid drug, Gel, Hydrocortisone, Topical use

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## INTRODUCTION

Hydrocortisone is one of the compounds that belong to the group of corticosteroids. It bears the scientific name hydrocortisone, hydrocortisone gel is of great pharmacological importance as it is widely used and has been licensed by the food and drug agency (FDA) in 1952<sup>1</sup> and one of its most important medical uses is used in the treatment of many different conditions, including allergies, skin conditions, ulcerative colitis, arthritis, lupus, multiple sclerosis, or lung disorders.

Hydrocortisone is also used to replace steroids in people with adrenal insufficiency (low production of natural steroids by the adrenal glands). Hydrocortisone affects your immune system and is often used to treat certain blood cell disorders such as anemia (low red blood cells) or thrombocytopenia (low platelets). Hydrocortisone is also used to treat some types of cancer such as leukemia, lymphoma, and multiple myeloma.<sup>2</sup> As the incidence of these diseases has increased, the prevalence of allergies and asthma has increased in almost all countries around the world and is more common in Western and economically developed countries. Up to one in three

individuals suffers from some form of allergic disorder.<sup>3,4</sup> A major pharmacokinetic profile of hydrocortisone gel is a highly potent glucocorticoid receptor agonist that possesses immunosuppressive, anti-inflammatory, and anti-proliferative effects. It acts by inhibiting phospholipase A2, which leads to inhibition of arachidonic acid synthesis and controls the biosynthesis of prostaglandins and leukotrienes.<sup>5,6</sup>

Hydrocortisone gel works by the following mechanism. The action of corticosteroids is to reduce the immune system's secretion of substances that cause dilation of blood vessels, redness, swelling, itching, and pain in the affected area. Reducing the migration of multinucleated leukocytes to the site of injury, in addition to reducing capillary permeability.<sup>7</sup> As for its topical uses, topical hydrocortisone is used for allergic dermatitis (DA) that occurs due to several factors, whether genetic or environmental. Hydrocortisone acts as an anti-allergic and anti-inflammatory, and it is also used to treat redness, swelling and itching and works by activating natural substances in the skin to reduce swelling, redness and itching<sup>8,9</sup> and one of the most important side effects of gel X

\*Author for Correspondence: suhadt.alakeli@uokufa.edu.iq

may occur stinging, burning, irritation, dryness or redness in the place of application. Acne, unusual hair growth, "hair bumps" (folliculitis), thinning or discoloration of the skin, or stretch marks<sup>10,11</sup> may also occur. Topical formulations containing hydrocortisone gel include the following containing ingredients: From HPMC K, tocopherol, 1% bisoprolol, carbopol, m-glycolate, citric acid and distilled water).<sup>12-14</sup>

## MATERIALS AND METHODS

Texture analyzer, multiple purposes topical formula analysis, China falling ball viscometer, models KF10 and KF20, comply with the German industry standard DIN 53015. Light microscope 1000X, Olympus, Japan for assessment. The transmission electron microscope, JEOL (Germany). Image processor for RGB analysis, USA. Centrifuge 5000 rpm, L-500, China, Sensitive balance (MediLife China), Remote thermometer (USA), VGA camera for image analysis, 20 MP Canon Japan. Thermal Camera,  $\pm 0.2$  C (Flur USA). pH meter (USA), HPLC, Cecil UK. UV V spectrophotometry Biotech Engineering management Co. Ltd. (UK), SHIMADZU FT-IR-8300 (MedLife India). Refrigerator, - 20°C, China. Magnetic stirrer UK.

### Preparation of the Gel Phase

Hydrocortisone gel consists of two phases, a gel phase, and a liquid phase.

The gel phase is prepared by preparation of 80 g of HPMC K6M in 200 mL of tocopherol and bisabolol is completed in a mechanical or magnetic mixing bowl containing 88 mL of distilled water with carbopol at 200 rpm for a period of 5 minutes at 25°C, then the mixture is heated to 45°C for one minute with continuous mixing. The temperature is reduced to 25°C, and the mixing continues for another 5 minutes, then 10 gm of glycolate, 5 gm of citric acid and 1% bisabolol are added, while the mixture is kept constant for another two minutes.

The liquid phase, it is prepared by adding 50% hydrocortisone to 8 gm of sodium glycolate and 2 gm of tocopherol, then adding the total with a mechanical mixer at a temperature of 25°C to 2 L of the gel phase and mixing at a speed of 200 rpm for a period of 3 minutes, then stopping for storage and canning directly.

## EVALUATION OF GEL (TABLE 1)

### The Color of the Formula

The color is measured in the in-kind method, and the color indicates the product quality index as the colors of some drug products.<sup>15</sup>

### The Odor

The smell is an important pharmacological characteristic of any product, because it is an indication of quality as well as an indication of the validity of the product such as gel, cream and ointments.<sup>16</sup>

### Appearance

It is the physical description that appears to the eye, such as the pure mixture, fluffy, transparent and opaque.<sup>17</sup>

### Homogeneity

It is tested to ensure consistency of appearance and if there are any materials collected in the gel after installing them inside the container and the product can be entered in repeated filtering steps to obtain homogeneity.<sup>18</sup>

### Viscosity

With a digital viscometer such as the Brookfield scale.<sup>19</sup>

### Spreadability

Spreadability is evaluated on the expansion scale. As the device is equipped with two square glass panels, 11 cm on both sides. On the outside of the bottom plate, a note sheet is attached to which it draws five concentric circles with a vertical diameter in millimeters. Propagation capability is determined as follows:

A 1 g of gel is placed between the plates and the upper plate is increasingly loaded with weights at equal time intervals

This standard is specified with a wooden block and a glass slide device. The gel (about 20 g) is added to the plate and monitors the time of the mobile top slide for complete separation from the constant. Spreadability of formulas is calculated as

$$S = W \times L/T$$

Where S = scalability, W = tide weight to the top slide, L = the length of the glass slide, and T = the time it takes to separate the slide from each other based on the results of 3 measurements, the arithmetic mean of the surfaces is drawn in the form of expansion curves. On Y, then coordinate the formatting surfaces, in  $\text{cm}^2$  and mark X as the value coordinates.<sup>20</sup>

### pH

Measurement of pH in water solutions from Gelusing a pH meter.<sup>21</sup>

### Rheology

The rheological property is determined to know the behavior of the gel flux. Viscosity is measured in rpm by Brookfield viscometer.<sup>22</sup>

### FT-IR Infrared Transformer Spectrum

The FT-IR study is used to verify the stability of active substances using infrared spectroscopy (Figure 1).<sup>23</sup>

### Grittiness or Sandy Quality

All microscopic gel formulations are evaluated for the presence of any concrete particles or under light microscopy. This makes the gel free of impurities and allow as desired for any topical preparation.<sup>24</sup>

### Determine Extrudability

Where the gel structures are filled in collapsible metal tubes. These tubes are subjected to pressure to extrude the materials and check the extrusion of the preparations. Extrusion of the preparation is determined by the weight in grams required to extrude a strip of gel of 0.5 cm in 10 seconds (Table 2).<sup>25</sup>

### Thixotropy

As it is possible for the gel to be converted to a soft texture after a period of time as a result of the weight factor and it is

**Table 1:** Results general pharmacological traits of the topical formula

<i>A) The general pharmaceutical test</i>	<i>Result</i>	<i>Statistics</i>
1. Color	Transparency 70%	56% whiteness $\pm$ 5%
2. Odor	Odorless	
3. Appearance	20% opacity	$\pm$ 3%
4. Homogeneity	Homogeneous sediment free	
6. Grittiness	No particles under the microscope	
7. Consistency	Emulsifying gel	
8. Swelling	No swelling after 3 month	
10. Thixotropy	80% flattening after 24 hours	
11. Dryness rate	No dryness	
14. Rheology	Easily flow	

**Table 2:** Results of the pharmacokinetic properties of the topical formula

<i>B) The objective pharmaceutical test of gel formula</i>	<i>Results</i>	<i>Statistics</i>
1. Viscosity	131 cps centipoise	1 $\pm$
2. Density	1.005	0.001 $\pm$
3. Spreadability	Score 1 easily spreadable	
4. Extrudability test	Score 3 good	
5. Microbial count	No microorganism per g	
6. pH value	6.9	0.1 $\pm$

**Table 3:** Results of diagnosing the topical formula with infrared and gel spectroscopy

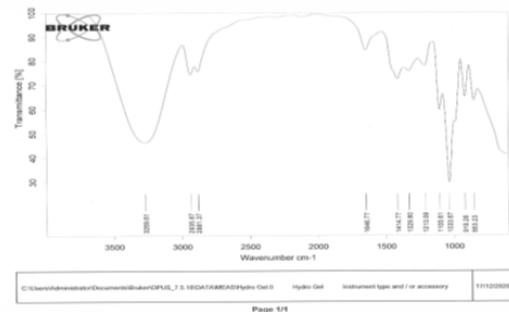
<i>C) Band documentation tests</i>	<i>Results</i>	<i>Comment</i>
1. FT-IR	10% alcohol shift as a difference in gel structure before and 24 months after production of the formula hydrocortisone gel	Used to assess the alcohol shift as an indicator of percentage of reactive conversion of the standard formula throughout a given period

traceable to the sides and its strength changes either by the weight stress or by the vibration or the external intensity.<sup>26</sup>

## RESULTS AND DISCUSSION

Proper drug selection and effective drug delivery is required for a therapeutic outcome in an optimal range. The controlled drug delivery technology has progressed immensely over the last six decades in the pharmaceutical industry. Lack of patient compliance is the major problem associated with conventional drug delivery systems.<sup>27</sup>

Gels are generally considered as a semisolid emulsion in an alcohol base, due to its cosmetic elegance it has a high rate of

**Figure 1 :** FT-IR Analysis

acceptance amongst consumers. Gels are generally thixotropic materials, exhibiting a stable form at rest but becoming fluid when agitated hence it shows better performance effect in terms of stability and therapeutic applicability.<sup>28</sup>

Topical steroid are recommended for atopic dermatitis and direct application to the painful site to provide local pain-relieving effect without the systemic adverse effects associated with oral steroid.<sup>29</sup> Topical application of gel formulation on the skin offer great advantage in a faster release of drug directly to site of action, independent of water solubility of the drug as compared to ointments and creams.<sup>30</sup> Stability studies formulation, which showed promising results, were subjected to stability studies at ambient room conditions for 3 months. After 3 months (90 days), no grittiness was found. Also, the homogeneity of the gels did not change. There was virtually no change in pH, drug release and viscosity. It indicates that the drug was stable in gels even after three months of short-term storage.

Hydrocortisone gel has been found to exhibit strong consistency, good homogeneity, spread ability, and viscosity parameters, pH varied between 6.8 to 7.1, no signs of grittiness were found (Table 2 and 3).

## CONCLUSION

From the above results it can be concluded that the steroid gel formulation was suitable for topical application. It is inferred from results that the gel formulation good in appearance, homogenate and easily spreadable. It has a clinical efficacy that compares well with much stronger preparations and should help to minimize the prevalence of harmful side effects of the treatment of distressing conditions.

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