Formulation, Characterization and Efficiency Evaluation of a Hydrogel Formulated with Algerian Thermal Water

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Abstract

Guergour thermal water (GTW) is commonly used in the east of Algeria for treating atopic dermatitis (AD) and psoriasis. Previous works demonstrated its chemical composition rich in minerals and heavy metals. The aims of the present study were (a) to possibly formulate a Hydrogel with GTW as an active agent (b) study the rheological properties and the stability of this Hydrogel (c) study the clinical efficiency of this Hydrogel towards atopic dermatitis symptoms.

First, several excipients with both inert physiochemical properties and ability to endure the high salinity of the thermal water were chosen. Second, a Hydrogel was formulated with the thermal water as the major component, carrying out rheological properties and stability studies. The Hydrogel was then tested on patients having AD problems during two weeks. For that, a comparative study was conducted with a Hydrogel with the same formula, but prepared with purified water as vehicle. The evolution of AD symptoms and signs were evaluated based on questionnaires for different considered patients.

The GTW being a thermal mineral water emerged with a neutral pH and a highly saline calcium sulfate. The Hydrogel formulated with GTW presented satisfactory rheological and sensory characteristics and was stable for 8 months under specific storage conditions. The clinical results revealed that 65% of AD patients showed significant improvements after the treatment, with partial sore disappearances.

This study provided the possibility to use the GTW as an active agent in a stable Hydrogel with therapeutic dermal effect. GTW-Hydrogel applied directly to the skin can be a key issue for AD patient caregivers.

Keywords: *Atopic Dermatitis; Guergour Thermal Water; Hydrogel; Rheology; Viscosity.*

I. Introduction

Atopic dermatitis (AD) is a common, highly inflammatory skin disease that starts early and can adversely impact the quality of life of patients and their caregivers [1]. In Algeria 5% of the population is suffering from AD [2].

The pathogenesis of AD is not completely understood. However the skin of individuals with AD has been shown to be deficient in lipid molecules that represent the first-line of defense against many infectious agents. These skin barrier abnormalities lead to transepidermal water loss and increased penetration of allergens and microbes into the skin [1]. Treatment of AD focuses on restoring the skin barrier and reducing flares [3].

In order to manage the condition, patients with AD necessitate applying frequently moisturizers as there is strong evidence that their use can reduce disease severity and the need for pharmacologic intervention [4].

Hydrogels are three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids [5]. They are biocompatible and used in numerous medical applications and pharmaceutical sectors, as drug delivery devices for example. This is due to their high water contents and soft consistency which is similar to natural tissue [6]. In 2008 Trookman *et al* found that the moisturizing desonide Hydrogel formulation would appeal to atopic dermatitis (AD) patients and potentially increase their treatment compliance comparing to other vehicle forms they have used in the past [7].

In Algeria since many years patients with AD are visiting Hammam Guergour (traditional hydrotherapy center) for the treatment of their dermatitis [8]. The beneficial effects of the water were put into evidence after clinical examinations of patients. GTW is highly mineralized natural water with a constant physicochemical composition, containing calcium, magnesium,

bicarbonate and rich in some essential trace elements.

The objective of this research is to develop a Hydrogel based on an Algerian thermal mineral water, where it were carried out characterization and stabilities studies as well as the effects on the skin were evaluated in vivo, to demonstrate the potential of thermal water in such systems.

II. Materials and methods

A. Materials

Hydroxy ethyl cellulose (HEC) was supplied by the Algerian pharmaceutical laboratory Biopharm (Algeria). Carbopol Ultrez 10, Glycerol, Triethanolamine (TEA) and propylene glycol were obtained from the Algerian cosmetic laboratory Venus. Thermal water came from Guergour source (Setif, Algeria). Distillated water was obtained locally.

Table 1. Ionic Composition of GTW (Mean ionic content per liter)

Sulfates	1669 mg	Potassium	8.0 mg
Chlorides	505 m	Silica	20mg
Sodium	353 mg	Zinc	0.473 mg
Bicarbonates	244 mg	Manganese	0.064 mg
Calcium	668 mg	Copper	<0.05 mg
Magnesium	111 mg	Iron	1.514 mg

Conductivity 3870 µs/cm
Mineralization2400mg/L

B. Hydrogel formulation

- Composition of GTW Hydrogel

At room temperature, the Carbopol Ultrez 10 was slowly added in small aliquots into the half amount of GTW with stirring to aid dissolution and gelation. The dispersion pH was adjusted to neutrality by adding TEA. Glycerol and Propylene glycol were added at the end. In the same way, HEC was dissolved at room temperature in the other half quantity of GTW, with stirring. After 2 hours, the dispersion of HEC was added to the first neutralized dispersion of Carbopol, with stirring. The sample of GTW-Hydrogel was neutralized to reach approximately a pH value of 7 and stored at 4°C until characterization.

- Composition of placebo Hydrogel

It was prepared with the same quantities and as described previously with using distillated water instead of GTW.

C. Rheological characterization of the Hydrogel

In the present work the rheological properties (viscosity) of each Hydrogel were studied and compared. Measurements were performed on an Anton Paar rheometer. The geometry used was a parallel plate, diameter= 25 cm. The gap was fixed at 1.0 mm. The rheological analysis of the GTW-Hydrogel was carried out at a continuous regime under variable shear, translated by the apparent viscosity η_{app}as a function of the shear rate$\dot{\gamma}$. The logarithmic ramp shear rate was varied from 10^{-3} to 10^{3} s $^{-1}$ with 04 decade measurement points and a measurement time sufficient to reach steady state.

D. Sensory analysis

Twenty volunteers, between 20 and 55 years of age with different healthy skin types had tested the GTW-Hydrogel. This method was done in standard conditions (temperature, 21°C; hygrometry, 45-50%). The volunteers had to evaluate each sensory characteristic by one of these levels: excellent, well, medium, bad.

E. Stability studies

To estimate the long-term stability of the GTW-Hydrogel, the sample was incubated at 4° and 25 °C ± 2 °C for 8 months. The GTW-Hydrogel was observed for any changes in the visual appearances (e.g. color change, phase separation, etc.) and in the rheological properties at regular intervals of time.

F. Clinical efficiency

The trials involved a group of twenty men and women (aged between 21 and 66 years) with moderate–severe AD. The patients were instructed to apply the placebo Hydrogel (based on demineralized water) and the GTW-Hydrogel on different eczematous inflammatory areas (EIA) of skin to dry, twice daily for 2 weeks. Use of any other emollient product was forbidden during the study. Patients were asked to fill out a questionnaire concerning the patient's bathing habits and the results were as shown in the next section.

III. Results and discussion

A. Chemical composition of GTW

The composition of GTW is shown in Table 1. This water had a thermal character, with 39°C of temperature and a pH close to the neutrality. Its total mineralization was 2400 mg.L^{-1}. It was sulphate-calcium water, bicarbonate sodium, containing many trace minerals (copper, zinc, etc.) which were necessary for the functioning and repair of dermal cells [9-11].

B. Rheological properties

Figure 1 shows the GTW-Hydrogel flow curve in terms of apparent viscosity as a function of shear rate. The curve shows a non-Newtonian rheological behavior of structural type, with the presence of a first Newtonian region, characterized by viscosity at the shear rate (η_0), a rheo-fluidifying intermediate behavior and an absence of the second Newtonian region [12]. The behavior was adjusted by Cross model as follows:

$$\eta = \frac{\eta_0}{1+(\frac{\dot{\gamma}}{D_{critical}})^n} \quad (1)$$

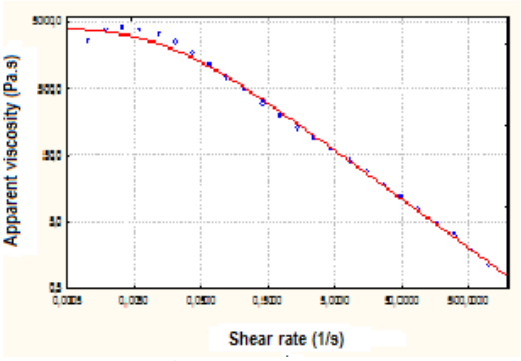

Figure 1. Flow curve of GTW-Hydrogel, T = 20 ° C.

C. Sensory test

The results of the study are shown in Table 2. The final evaluation of each sensory property was done by adding the percentages between excellent and well and the percentages between medium and bad. According to the evaluation report, 85% of volunteers appreciated the softness of GTW-Hydrogel and 85% found it easy spreading. At this time, 25% found that GTW-Hydrogel was sticky, 80% of them liked its texture. The weighted average score assigned to the Hydrogel by all evaluators was 81.25%.

Table2. Sensory evaluation sheet of the GTW-Hydrogel

	Excellent	well	Medium	Bad
Product Texture	07	09	02	02
Spread	10	07	02	01
Softness	05	12	03	02
Sticky effect	06	08	04	01

D. Stability of GTW-Hydrogel

The formulated Hydrogel was stable for 8 months under both storage conditions of 4 and 25°C. Figure 2 shows the flow curve in terms of apparent viscosity as a function of shear rate of the same formulation Hydrogel stored at 4°C for 8 months.

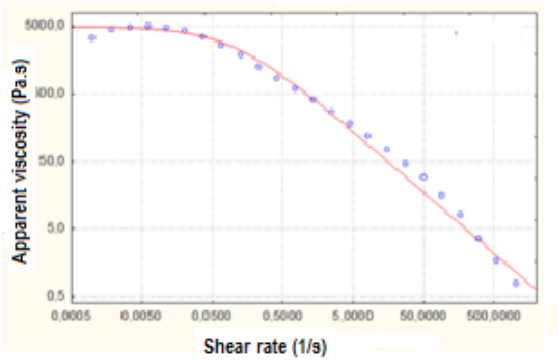

Figure 2. Flow curve of GTW-Hydrogel stored at 4°C for 8 months, T = 20 ° C.

Clearly, the shape of the curve is similar to that in Figure 1. This confirms the stability of the Hydrogel.

E. Clinical efficiency

The comparative analysis showed that 65% of patients confirmed a significant reduction of inflammation, a loss of crusts and redness in the areas treated with GTW-Hydrogel with a satisfaction of their emollient and soothing effects. 35% of patients did not notice any positive effect of the product, and 67% patients responded positively to the emollient and soothing effect of placebo (Figure 3).

Figure 4 shows the clinical effects of GTW-Hydrogel tested on a patient. It showed that by the end of the trial, the redness of EIA was less on the region where the GTW-Hydrogel was used after 15 days.

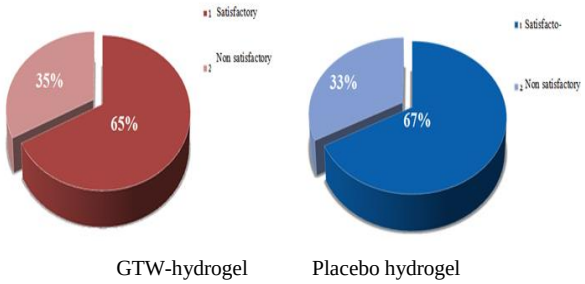

Figure 3.Representation of rate of satisfied patients with respect to the bio-gels

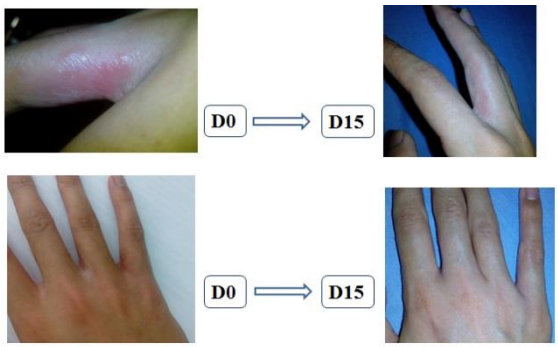

Figure4. Clinical improvement of AD. Pictures were taken before (D0) and after a 2-week GTW-Hydrogel therapy (D15)

IV. Conclusion

Clinical experience has proved GTW-Hydrogel applied directly to the skin can be an effective and safe auxiliary treatment for dermal diseases.

This Hydrogel will help patients to get the benefits of the Guergour thermal waters without going to the hydrotherapy center. We believe that their use will help patients to improve their quality of life.

Furthermore, according to the therapeutic qualities exhibited by this Hydrogel and the developed dermo cosmetic product, it could be also of great interest to use in specific dermatological diseases, like psoriasis.

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Abbreviations

AD Atopic Dermatitis
EIA Eczematous Inflammatory Areas
HEC Hydroxyethylcellulose
GTW Guergour Thermal Water

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