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Aloe Vera as Topical Hydrogel; Formulation and Rheological Assessment

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ABSTRACT

Aloe is a genus containing over 500 species of flowering plants. The most widely known species is Aloe Vera [AV], which mainly used internally and externally on humans as alternative medicine. The commercial topical dosage form has some limitations as absorption variability, short retention time, and improper viscosity and consistency. This research aimed to reformulate AV as a topical hydrogel, to assess the rheological properties of this formulation, and to study the effect of storage on its rheological properties. AV hydrogel different formulation was prepared by using 0.5, 1, and 2% Carbopol 934 as a gelling agent in different concentrations. The rheological properties as viscosity, Farrow's constant, and rheological behaviors were determined. The effect of storage for twelve-month on the rheological properties was also performed. The results indicate that direct and non-linear relation between the concentration of carbopol 934 and the estimated viscosity of the hydrogel. The viscosity ranged from 9073 -936451 cp, which is suitable for topical application, the Farrow's constant was > 1; which confirmed the pseudoplastic flow with a thixotropic behavioral rheology. The effect of storage of formulation for 12 months has no significant effect on all rheological parameters at $p \leq 0.5$, which indicated the stability of the prepared hydrogel. AV successfully prepared as a topical hydrogel; this formula will help in the elimination of improper consistency associated with topical marketed products. The rheological assessment indicated the suitability of the prepared formulation for topical application, the excellent stability in flow properties against storage for a prolonged period, and the formulation exhibited pseudoplastic flow with thixotropic behavioral rheology.

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INTRODUCTION

Aloe Vera is one of Aloe plant species (Kim *et al.*, 2000). The active principles present in this plant species usually exert their action through the anti-inflammatory, moisturizing, and antioxidant effect on human skin Hamman (2008). Due to the presence of several elements and vitamins in their composition (Bozzi *et al.*, 2007; Olaleye and Bello-Michael, 2005; Chithra *et al.*, 1998). Challenge in using topical commercially available Aloe Vera is the improper consistency due to difficult flow properties of some product and low viscosity for others (Feily and Namazi, 2009), Another challenge is the short retention time after application on the surface of skin which limits its absorption and its moisturizing effect (Sato *et al.*, 1990). For that reason, reformulation of this aloe extract as a topical dosage with suitable consistency is recommended.

Gels are classified according to the vehicle into hydrogels or organogels (Ahmed, 2015). A hydrogel is a colloid dispersion in which the dispersed phase (colloid or gelling agent) has combined with the continuous dispersion media (water) to produce a viscous jellylike product (Richter *et al.*, 2008). According to the colloidal phase, the gelling agent may be inorganic as bentonite or organic as carbomers. Carbopol is a synthetic high molecular weight polymer of acrylic acid that is crosslinked with either allyl sucrose or allyl ether of pentaerythritol (Kulkarni and Biswanath, 2007). They contain between 56% and 68% of carboxylic acid groups calculated on a dry basis. They are formed from repeating units of acrylic acid. They used as a gelling agent in a concentration ranging from 0.5-2% (Singla *et al.*, 2000).

Thixotropic behavior which known as sol-gel-sol transformation in material consistency, when accompanied with the pseudoplastic polymeric character which known as shear-thinning materials, this behavior allow the polymeric dispersion to be in fluent state under shear, and after removal of this stress, the viscosity increase again and the dispersion return to its gel form (Oppong *et al.*, 2006; Edsman *et al.*, 1996). A preferred example of a material altering viscosity from a liquid to a gel upon exposure to shear or other physical forces is the naturally occurring hyaluronic acid (Lee *et al.*, 2009). Most of the pharmaceutical topical formulation preferred to exhibit pseudoplastic rheological properties to ease its application (Santoro *et al.*, 2011). After use, it is preferred that the viscosity return increase to specific limit to decrease the drainage of the product out of its application site, which confirmed in rheology by the term thixotropic behavior (Tan *et al.*, 2000).

This research aimed to reformulate AV as a topical hydrogel, to assess the rheological properties of this formulation, and to study the effect of storage on its rheological properties.

MATERIALS AND METHODS

Aloe Vera was kindly gifted from EIPICO (Cairo, Egypt). Carbopol 934 was purchased from Sigma Chemical Company (St. Louis, Missouri, USA). Phosphate buffer saline kit, and triethanolamine were purchased from Fluka Chemicals (Buchs, Swit- zerland). All other chemicals and reagents used in the study were of analytical grade.

Preparation of Aloe Vera Gels

Aloe Vera powder was dissolved in phosphate-buffered saline to prepare a solution of concentration 10 mg/ ml with the aid of sonication. The weighed amount of Carbopol 934 was sprinkled gradually, into the vortex of 100 ml Aloe Vera solution, and stirred with a mechanical stirrer until no observed lumps at high, stirring speed. Then the speed of stirring was decreased to break and remove the formed foam, then one-milliliter triethanolamine was added at once to form the gel; care was taken to avoid the formation of air bubbles. Carbopol 934 gel bases were prepared at concentrations of 0.5% (F1), 1% (F2) and 2% (F3).

Investigation of the rheology of Aloe Vera freshly prepared gel formulations

The viscosities of different gel formulae were determined using Brookfield Viscometer, spindle 52 at 25°C. One gram sample was tested from each formula. In order to identify the flow behavior of each gel, the viscosity was determined at a different rate of shear (2, 10, 20, 30, 40, 50, and 60 sec^{-1}). The shear rate in sec^{-1}, shear stress in dyne/cm^2, and the viscosity in centipoise were determined. The rheological parameters of different gel bases were studied, in which the viscosity of each formula at a minimum rate of shear (η_{min}) and a maximum rate of shear (η_{max}) were determined. To study the flow behavior of the different gel bases, apply Farrow et al. equation:

$$Log\ G\ =\ N\ Log\ F\ -Log\ \eta$$

Where: G is the shear rate (sec^{-1})

F is shear stress (dyne/cm^2)

η is viscosity (c.p.)

N is Farrow's constant

To obtain the value of N (slope), which indicates the deviation from Newtonian flow, log G was plotted against log F

Investigation of the rheology of Aloe Vera formulations after storage for 12 months

The different gel formulae were stored in dark bottles at room temperature for 12 months. The viscosities of different gel formulae were determined again after storage using the same experimental conditions used before the storage, and the rheological parameters of different stored gel bases were assessed.

Assessment of thixotropic behavior of the prepared gel formulation

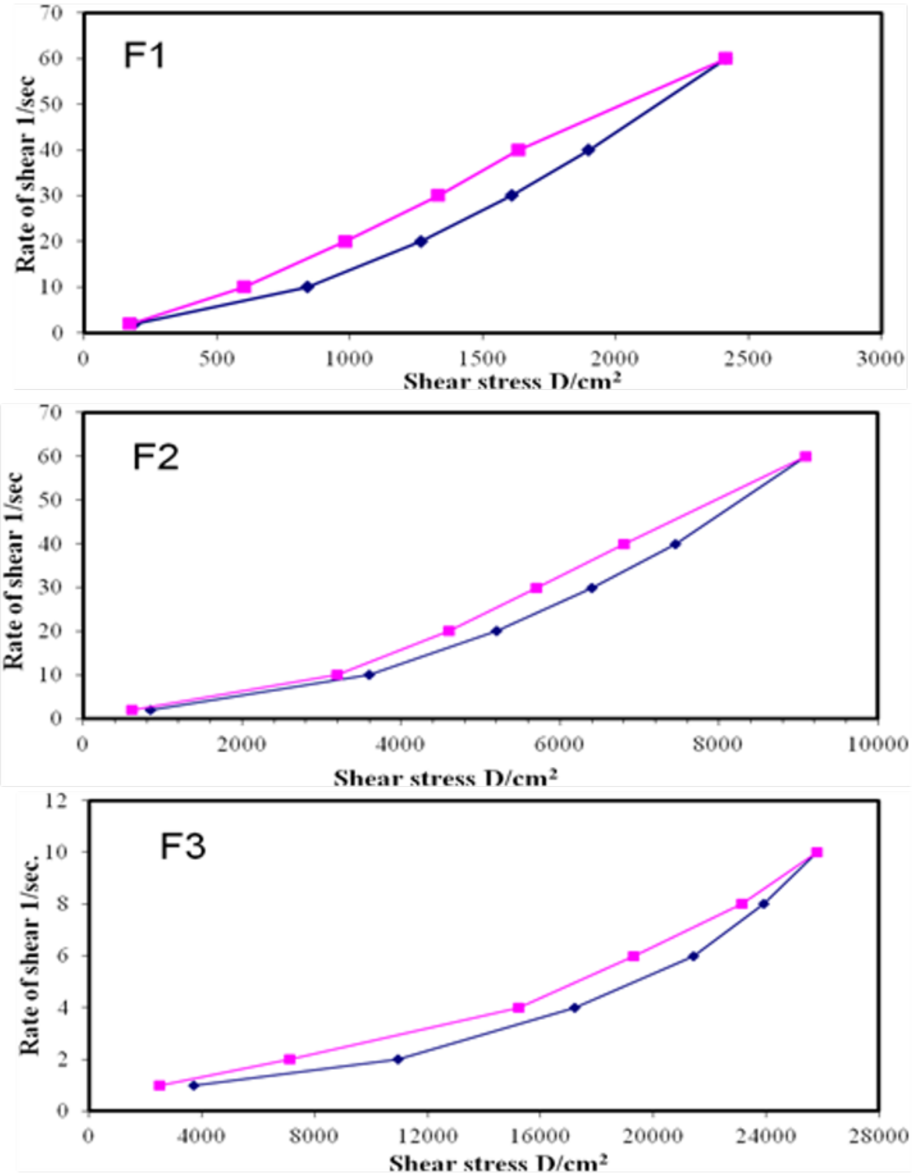

Figure 1: Rheograms of the different freshly prepared AloeVera gel formulations

Table 1: Rheological Parameters of Different Aloe Vera Gel Formulations.

Formula Number	Viscosity (min.) (c.p)	Viscosity (max.)(c.p)	Farrow's constant	Flow Behavior
F1	9073±303	3704±243	1.3237	Pseudoplastic
F2	123540±1435	14764±1142	1.4075	Pseudoplastic
F3	936451±3924	284512±2435	1.8302	Pseudoplastic

Table 2: Rheological Parameters of Different Aloe Vera Gel Formulations after storage for 12 months at room temperature.

Formula Number	Viscosity (min.) (c.p	Viscosity (max.)(c.p)	Farrow's constant	Flow Behavior
F1	9214±264	3804±349	1.4114	Pseudoplastic
F2	141245±1256	24157±1089	1.4996	Pseudoplastic
F3	947451±3743	315478±4817	1.9877	Pseudoplastic

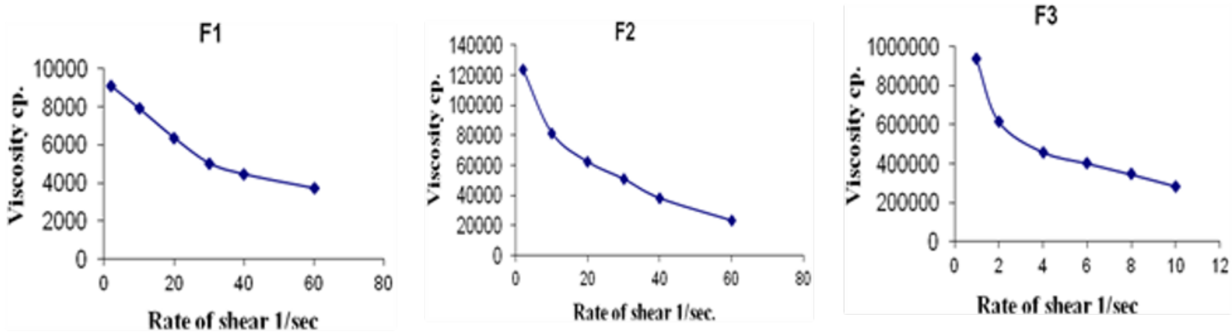

Figure 2: Plotsof the rate of shear (G) versus viscosity (η) for AV different freshly prepared gel formulations.

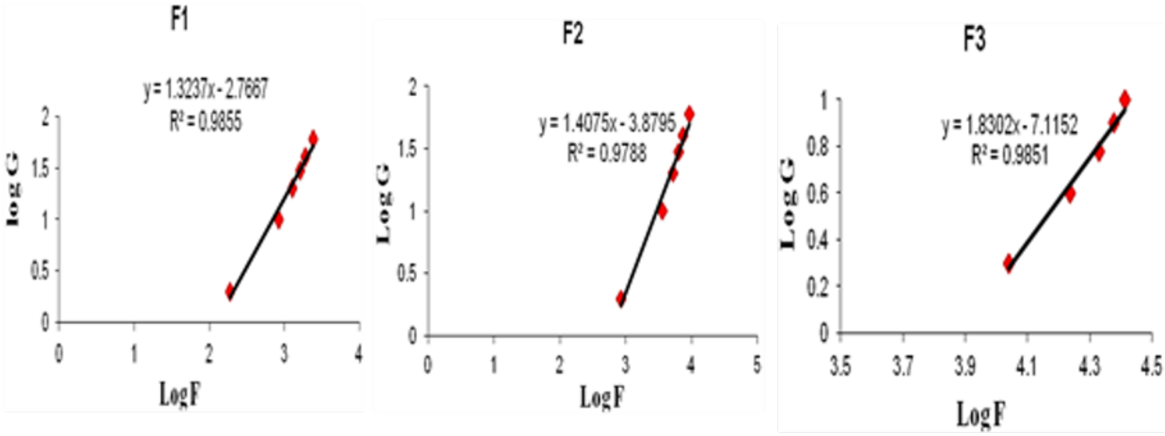

Figure 3: Plots of Log Rate of Shear (G) Versus Log shearing Stress (F) for AV different freshly prepared gel formulations.

In order to identify the thixotropic behavior of each gel, the viscosity was determined at a different rate of shear (2, 10, 20, 30, 40, 50, and 60 sec^{-1}). Then the rate of shear was decreased gradually in descending order at the same point of measure used in the ascending order. The shear rate in sec^{-1}, shear stress in dyne/cm^2, and the viscosity in centipoise were determined. And the program shows the relation between the shear rate and shear stress were illustrated. From the program, the degree of thixotropy was calculated by measuring the area of hysteresis loop according to the following equation [area of hysteresis loop = AUC of the up-curve / AUC of the down-curve]. Data were expressed as mean $\pm$ S.E... They were statistically analyzed using analysis of variance (ANOVA) at a level of p $\leq$ 0.5 using the SPSS program to show the differences between the parameters before and after the storage.

RESULTS AND DISCUSSION

Aloe Vera moisturizer different gel formulae which prepared with varying concentrations of carbopol 934 were inspected visually for their color and syneresis. The developed AV gel formulations were much clear, transparent, and showed good homogeneity with the absence of lumps, bleeding, and syneresis. And this inspection, when repeated after storage for twelve months at room temperature, ensured the stability of all formulation. No significant change was observed in the parameters evaluated like physical appearance as to color, syneresis, and rheological properties.

The evaluation of the rheological properties of the gels as a dosage forms would be important for predicting their behavior in-vivo. (Lee *et al.*, 2009; Santoro *et al.*, 2011).

It is clear from the obtained result that by increasing the concentration of polymeric material in gels, there was an increase in viscosity values, for Carbopol 934 gel base the η_{min} for formula F3 (936451 cp) > F2(123540 cp) > F1(9073 cp)

Rheograms of the prepared gel formulations were plotted; Y-axis was taken to represent the shear rate and X-axis to represent the shear stress, as shown in

Figure 1.

The flow behavior of different gel bases, as described in Table 1. From the data of the table, all gel bases exhibited pseudoplastic flow with a thixotropic behavior, which is a desirable character in pharmaceutical gels.

Table 1 shows the viscosity of each formula at a minimum rate of shear (η_{min})and a maximum rate of shear (η_{max}). It clear that for each formula, the η_{max} is less than η_{min}. So, there is a structural breakdown of the polymeric chains during shear.

Figure 2 showed the relation between the viscosity and shear rate of different gel bases at various concentrations.

It should be noted that there was an inverse relationship between shear rate and viscosity. So, a typical pseudoplastic flow was obtained.

To obtain the value of Farrow's constant (N), which indicates the deviation from Newtonian flow, log G was plotted against log F, and N obtained from the slope, as shown in Figure 3**.**

It is clear from the result that N is greater than one, indicates pseudoplastic flow "*shear rate thinning*." This could be due to the structural breakdown of the existed intermolecular interactions between polymeric chains during shear exerted, and after removal of the shearing force, the polymerization is reoccurred due to van der Waal interaction forces occur between the polymer molecules. (Chittodiya *et al.*, 2013; Rudraraju and Wyandt, 2005).

In order to ensure the stability in the rheological behavior of the prepared AV gel formulations, the rheological assessment was repeated for all formulation after storage at room temperature for twelve months. Table 2 indicated that AV different gel formulation showed excellent stability regarding the rheological behavior. The η_{min} for formula F3 (947451 cp) > F2(141245 cp) > F1 (9214 cp),

It is clear that all gel formulation still exhibited pseudoplastic flow with a thixotropic behavior, which is a desirable character in pharmaceutical gels (Hoshizawa *et al.*, 2013). This confirmed that there is no significant effect at $p \leq 0.5$ for twelve-month storage at room temperature on rheological properties of all prepared AV different gel formulations prepared by different concentrations of carbopol 934.

CONCLUSIONS

Due to challenges facing the use of most of the commercially available topical moisturizer of Aloe Vera, which include; improper consistency and short retention time on the skin surface, reformulation of this natural moisturizer as topical dosage form with suitable consistency is recommended. The rheological behavior of the freshly prepared different gel formulation made by use of carbopol 934 as a gelling agent revealed that they exhibited a pseudoplastic flow with thixotropic behavior i.e., increasing shear rate leads to decreasing the viscosity, which is a desirable character in pharmaceutical gels. There was no effect of storage for twelve months at room temperature on rheological properties of all prepared formulations, and the results revealed that they still exhibited a pseudoplastic flow with thixotropic behavior.

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