# DERMATOCOSMETICS FACIAL MASKS FOR TOPICAL TREATMENT OF ACNE

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Acne is one of the most common skin diseases affecting mostly adolescents, but can occur also into adulthood. Acne can have profound psychological and social effects, not only for high severity acne, but even in less severe cases. *Staphylococcus epidermidis* (*S. epidermidis*) bacteria and *Propionibacterium acnes* (*P. acnes*) bacteria are considered to cause this disease. Over time they have used many treatments for acne especially antibiotics, metronidazole showing positive effects and long-lasting. Thus, the purpose of this study was to design and investigate some facial masks in form of membranes with collagen and metronidazole to reduce and prevent adverse effects of conventional treatments using for acne. Type I fibrillar collagen gel was the main component of all masks. Hydrogels based on collagen, metronidazole, starch and polyvinilpyrolidone showed a pseudoplastic behavior with yield stress facilitating their flow and allowing their good manipulation. The membranes were obtained by drying the hydrogels in controlled environment and characterized by water absorbtion and enzymatic degradation. The results relieves that the presence of polymers (starch and polyvinylpirolidone) influence the stability and integrity of the membranes obtain. Based on these results, we could conclude that the obtained masks are potentially usable as a favorable solution in acne disease.

Keywords: acne disease, collagen, masks.

## INTRODUCTION

Acne is one of the most common skin diseases affecting mostly adolescents, but can occur and adulthood. Worldwide, about 85% of young people aged between 12 and 25 years are affected by acne (Kim and Michaels, 2012). In Romania, over 90% of adolescents have acne, 50% of adult women, 25% of all adults, regardless of gender, suffer from acne, according to studies by Romanian Society of Dermatology. This disease affects the skin of the face, the neck and the upper torso, forming non-inflammatory lesions (comedones) or inflammatory lesions (papules, pustules and nodules). *Staphylococcus epidermidis* (*S. epidermidis*) and *Propionibacterium acnes* (*P. acnes*) bacteria that are considered main cause of this disease (Sawarkar *et al*., 2010). Genetic and environmental factors contribute to the pathogenesis of acne (Ballanger *et al*., 2006).

Nowadays different topical therapies are available for patients with acne, including comedolytic agents, anti-inflammatory medications, antibiotics, and even herbal preparations. Metronidazole, an imidazole, is an antibacterial agent that has been shown to be effective in reducing acne inflammation when is administered orally or in form of

an aqueous gel for topical application. Its mechanism of action in acne is thought to be associated with its anti-inflammatory, immunosuppressive, and antimicrobial properties (Khodaeiani *et al*., 2012). Studies have shown that metronidazole can be released in a sustained manner for a period of one week. This study aimed to evaluate the efficacy of 0.95% metronidazole in combination with 1% collagen in a facial mask for the treatment of acne. Collagen has become an important component in cosmetics formulations providing numerous benefits. In particular, collagen is a natural humectant efficient because of the hydration orderly sphere that surrounds the molecule (Peng *et al*., 2004). Regarding acne, there are studies that claim that collagen degradation is responsible for acne scars, healing them being related to the rearrangement of collagen fibers (Fabbrocini *et al.*, 2012).

The aim of this study is to obtain and characterize collagen-metronidazole masks for treatment of acne.

## MATERIALS AND METHODS

### Materials

Type I fibrillar collagen gel (Coll) was extracted from calf hide with initial concentration of 2.84 % (w/w), using technology previously described (Albu, 2011). Glycerine (GL) was purchased from Romaqua Holdings, Romania, Ethanol (ET) from Chemreactiv S.R.L., Romania, Metronidazole (MN) from Hubei Hongyuan Pharmaceutical technology Co.,Ltd., China, Starch (ST), Polyvinylpirolidone (PVP) and Glutaraldehyde (GA) from Merck, Germany, *Collagenase* from Sigma Aldrich, Germany and Sodium hydroxide from Lach-Ner, Czech Republic.

### Collagen Hydrogels and Masks Preparation

Collagen hydrogels were obtained by continuous stirring of gels adjusted at 1% and 7.2 pH, using 1M sodium hydroxide, with glycerine, ethanol, and added different concentrations of metronidazole, starch and polyvinylpirolidone, reported to collagen dry substance, as it is shown in Table 1. Then, all the gels were crosslinked with a specific amount of glutaraldehyde (0.5% reported to collagen dry substance), cast in Petri dishes resulting hydrogels which were dry in oven at 37°C, obtaining collagen membranes - masks.

Table 1. Collagen hydrogel compositions

| Code of gels | Coll, % | GL, % | ETH, % | MN, % | ST, % | PVP, % | GA, % |
|---|---|---|---|---|---|---|---|
| G1 | 1 | 2.53 | 7.2 | - | - | - | 0.5 |
| G2 | 1 | 2.53 | 7.2 | 1.26 | - | - | 0.5 |
| G3 | 1 | 2.53 | 7.2 | 1.26 | 0.26 | - | 0.5 |
| G4 | 1 | 2.53 | 7.2 | 1.26 | - | 0.26 | 0.5 |

### Methods of Analyses

*Rheological Analysis*

The rheological measurements were conducted at 37$^{o}$C with a rotational viscometer MultiVisc-Rheometer, Fungilab equipped with a standard spindle TR 9 and an

Ultrathermostat ThermoHaake P5 to keep constant the temperature during the experiments. The operational conditions for rheological determinations were detailed in our previous studies (Ghica *et al*., 2012).

The rheograms shear stress versus shear rate was built. For the quantification of the flow behaviour, different rheological models were used: *Casson* (eq. 1), *Bingham* (eq. 2), *Ostwald-de Waelle* (eq. 3) and *Herschel-Bulkley* (eq. 4) (Albu, 2009) and the determination coefficients ($R^2$) values were used as an indicator to chose the one that best fitted the flow profiles (Paunica-Panea *et al*., 2016).

$$\tau^{0.5} = \tau_0^{0.5} + \eta^{0.5} \cdot \dot{\gamma}^{0.5} \quad (1)$$

$$\tau = \tau_0 + \eta \cdot \dot{\gamma} \quad (2)$$

$$\tau = K \cdot \dot{\gamma}^n \quad (3)$$

$$\tau = \tau_0 + K \cdot \dot{\gamma}^n \quad (4)$$

where, $\tau$ is the shear stress (Pa), $\dot{\gamma}$ – shear rate ($s^{-1}$), $\eta$– plastic viscosity (Pa·s), $\tau_0$– yield stress (Pa) related to the minimum stress to be applied for determining the start of hydrogel flow, K – consistency index (Pa·$s^n$) associated with the hydrogel viscosity, n – flow behavior index indicating the flow profiles ((Paunica-Panea *et al*., 2016; Ghica *et al*., 2016).

*Water Up-take*

Collagen membranes obtained by drying in oven were tested by water up-take. They were firstly immersed in water at 36°C then withdrawn and weighed at fixed time intervals. The equation used (eq. 1) for water absorption determination was:

$$\%Water\ up\text{-}take = (Wt - Wd)/\ Wd\ (g/g) \quad (5)$$

where Wt is the weight of the swollen samples at immersion time t, and Wd denotes the weight of the dry samples. All the samples were studied in triplicate.

*Enzymatic Degradation*

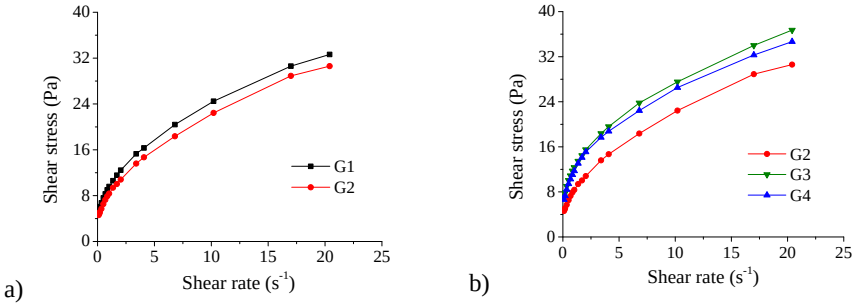
Enzymatic degradation of collagen membranes was investigated by monitoring the weight loss depending on exposure time to collagenase solution. Small pieces of collagen membranes were accurately weighed, placed in collagenase (1 $\mu$g/mL) and incubated at 36°C. At regular time intervals, the swollen membranes were removed from degradation solution and weighted. The percentage of membrane degradation was determined by the following relation:

$$\%\ weight\ loss = (Wi - Wt)/Wi*100 \quad (6)$$

where *Wi* is the initial weight and *Wt* is the weight after time t.

## RESULTS AND DISCUSSION

The influence of the hydrogels composition on the rheological profiles plotted as shear stress as a function of shear rate is presented in Figure 1a and 1b.




a) b)

Figure 1. The flow profiles recorded at 37°C for hydrogels

a) G1 and G2 b) G2, G3 and G4

The rheograms recorded in Figures 1a and b shown a non-Newtonian behaviour, the shear stress increasing with shear rate increase. The determination coefficients R2 obtained for the rheological models (eqs. 1-4) mentioned at Materials and Methods section are given in Table 1.

Table 1. The determination coefficients values of different rheological models for hydrogels G1-G4 analyzed at 37°C

| Rheological models | R2 values | | | |
|---|---|---|---|---|
| | G1 | G2 | G3 | G4 |
| Casson | 0.9878 | 0.9901 | 0.9856 | 0.9881 |
| Bingham | 0.9421 | 0.9504 | 0.9317 | 0.9227 |
| Ostwald-deWaele | 0.9937 | 0.9939 | 0.9937 | 0.9959 |
| Herschel-Bulkley | 0.9994 | 0.9994 | 0.9998 | 0.9996 |

As can be seen in Table 1, the highest values for R2 were obtained for Herschel-Bulkley, indicating that this model best fitted the rheological experimental data. The parameters characteristic for this model are presented in Table 2.

Table 2. Rheological parameters specific to Herschel-Bulkley model for hydrogels G1-G4 tested at 37°C

| Rheological parameters | Hydrogels | | | |
|---|---|---|---|---|
| | G1 | G2 | G3 | G4 |
| Yield stress (Pa) | 3.207 | 2.472 | 4.277 | 3.358 |
| Consistency index (Pa·sn) | 6.421 | 5.588 | 7.962 | 8.358 |
| Flow index | 0.509 | 0.538 | 0.465 | 0.438 |

The values recorded for flow index are smaller than 1, indicating a pseudoplastic behavior. The adding of metronidazole in formulation G2 determined a decrease of yield stress about 23% and of consistency index about 13% respectively, in comparison with hydrogel G1. The presence of starch and PVP in hydrogels formulation G3 and G4 led to an increase of yield stress about 1.73 and 1.36 times respectively comparing to

hydrogel G2, while for the consistency index the increase was aproximately 1.42 and 1.50 times respectively.

The results of water up-take studies are presented in Figure 2.

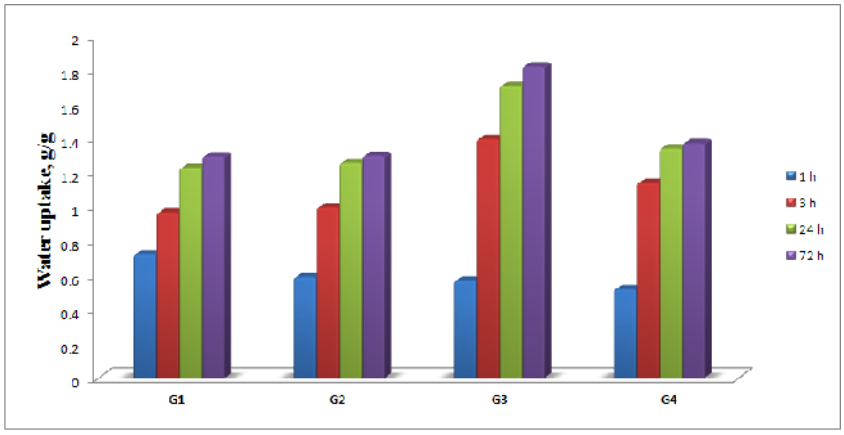



Figure 2. Water up-take for collagen membranes

Figure 2 showed that swelling was influenced by the presence of polymers added in each membrane. The highest water up-take was recorded for membranes which have starch in composition, this being the most hydrophilic one. The metronidazole and PVP did not influence too much the water up-take, having similar values. Also the difference of water up-take after one and three days is not too high, showing the stability of the membranes.

The results of enzymatic degradation presented in Figure 3 showed that de membranes degraded up to 15.23% (G3) in first hour.

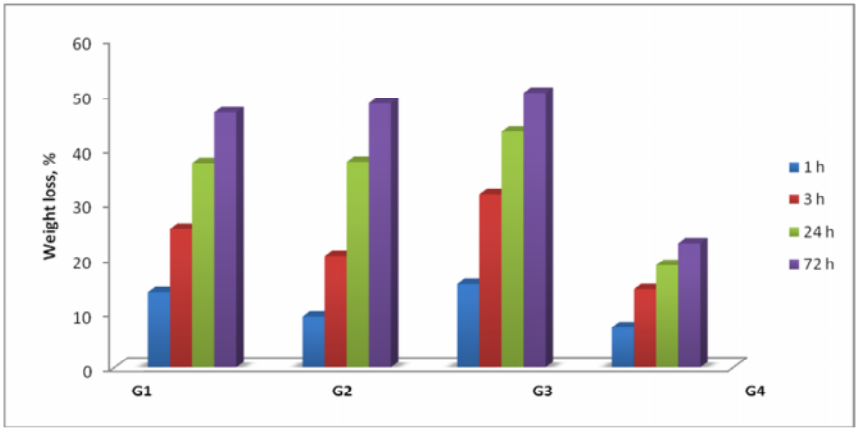



Figure 3. Enzymatic degradation for collagen membranes

After one day, G1 and G2 degraded about 37% and G3 about 43%. These results are in accordance with water up-take and it was expected for sample G3, which was the

most hydrophilic to be fast degradable. The samples containing PVP showed the best resistance to collagenase solution, PVP being a good stabilizer in cosmetics. The results of degradation are in correlation with rheological and water up-take results.

## CONCLUSIONS

Collagen hydrogels with metronidazole and polymers (starch and polyvinil-pyrolidone) were prepared and rheologically analysed in ordor to be used for masks preparation. Rheological studies show that all the designed hydrogels presented a pseudoplastic character with yield stress facilitating their flow and allowing their good manipulation. Absorbtion and enzymatic degradation studies relieves that the presence of polymers (starch and polyvinylpirolidone) influence the stability and integrity of the membranes obtain. Based on these results, we could conclude that the membranes obtained are potentially usable as a dermatological masks for treating acne disease.

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