RESEARCH ARTICLE

# Experimental Research for Gelator Selection in the Development of a Medicine for the Treatment of the Second Degree of Acne

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## Abstract

**Aim:** The aim of this study is to develop a stable gel base with fusidic acid and to study its structural and mechanical properties. **Materials and Methods:** Structural and mechanical studies were conducted on a Brookfield DV-II + PRO viscometer with a rotary spindle SC4-21 (USA). The structural viscosity ŋ (mPa • c) and the shear stress τr (Pa) were measured at different shear rates of Dr or γ ($c^{-1}$). With this instrument, the following parameters were measured. Colloidal stability was determined by means of a laboratory centrifuge OPN-12 of the company "TNK DASTAN" (RF). The pH value of the investigated foam samples was determined potentiometrically (DFU 1.2, 2.2.3) using the "pH meter Metrohm 744" device (Germany). **Results and Discussion:** The structural-mechanical and physical-chemical properties of gels with 2% fusidic acid on the basis of promising gelators were investigated, namely: Hydroxyethylcellulose, xanthan gum, sodium alginate, guar gum, and carbomer Ultrez-10 NF. **Conclusions:** It was proved that the best structural, mechanical, physical, and chemical consumer properties were based on a mixture of xanthan and sodium alginate. The mechanical stability indicators were calculated on the basis of structural and mechanical studies, which indicate positive extrusion properties of the selected base with fusidic acid and confirm its stability during storage (for 2 years). It was shown that a gel with fusidic acid based on a mixture of xanthan and sodium alginate represents an elastic-viscoplastic system with moderate thixotropic properties that provide the necessary extrusion and technological properties, as well as corresponding satisfactory consumer characteristics.

**Key words:** Acne, fusidic acid, gel, gel base, structural viscosity

## TOPICALITY

Acne is the most common skin disorder affecting 85% of people aged 12 to 25 years and 11% of people aged 25 years and older.[1-5]

Unfortunately, this disease can, in the absence of or inappropriate treatment, result in the formation of drawn scars, especially in the second and third degree of acne. It would be desirable to note that also medicines on the basis of hydrophobic substances (lanolin, vaseline, etc.) are not recommended in the treatment of second and third degrees of acne, which tend to block the pores of the skin and to form new conglomerates.[6-10]

In pharmacotherapy of drugs for the treatment of acne, soft drugs are used - gels, emulsions of type oil/water and cream-gels, which provide maximum release of active substances.[11-13]

Today, a number of active pharmaceutical ingredients, in particular a number of antibiotics, are used in the development of modern medicines for the treatment of acne. Fusidic acid

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gives good results for treating second and third acne when used externally. Fusidic acid has a high penetrating ability and a wide range of action against microorganisms that cause the disease.

The work was aimed at developing a stable gel base with 2% fusidic acid for local treatment of second degree acne and studying its structural and mechanical properties.

## MATERIALS AND METHODS

As the research object, gel samples with fusidic acid were selected based on a number of gelators of different origin hydroxyethyl cellulose ("Ashland," USA), xanthan ("Foodchem International Corporation," China), sodium alginate ("FMC BioPolymer," USA), Guar ("Economy Polymers and Chemicals," USA), Ultrez-10 NF carbomer ("Lubrizol"), USA and purified water. Glycerin was used to quickly obtain gel bases with natural gelators (our article about gelators).

Structural and mechanical studies were conducted on a Brookfield DV-II + PRO viscometer with a rotary spindle SC4-21 (USA). The structural viscosity ŋ (mPa • c) and the shear stress τr (Pa) were measured at different shear rates of Dr or γ ($c^{-1}$). To objectively evaluate the reo parameters, the coefficients of dynamic dilution (Kd) and mechanical stability (MS) of gel specimens were calculated based on the data obtained. The study was conducted at room temperature (DFU). With this instrument, the following parameters were measured.

Colloidal stability was determined by means of a laboratory centrifuge OPN-12 of the company "TNK DASTAN" (RF).

The pH value of the investigated foam samples was determined potentiometrically (DFU 1.2, 2.2.3) using the "pH meter Metrohm 744" device (Germany).

Present studies were conducted on the premises of the scientific laboratory of the Department of Commodity Science at the National University of Pharmacy.

## RESULTS AND DISCUSSIONS

At the first stage, the purpose of the study was to justify the choice of the gelator.[11,12]

For the preparation of gel bases, the following gelators were chosen: A carbomer of the brand Ultrez 10 (neutralizer - 10% solution of sodium hydroxide) - base number 1, xanthan - base number 2, guar - base number 3, xanthan: sodium alginate - base number 4, sodium alginate - base number 5, and hydroxyethyl cellulose - base number 6.

| Base No. 1 | |
|---|---|
| Carbomer Ultrez 10 NF | 0.5 |
| Sodium hydroxide (10% solution) | 0.5 |
| Purified water | Up to 100.0 |

| Base No. 2 | |
|---|---|
| Xanthan | 2.0 |
| Glycerin | 5.0 |
| Purified water | Up to 100.0 |

| Base No. 3 | |
|---|---|
| Guar | 2.0 |
| Glycerin | 5.0 |
| Purified water | Up to 100.0 |

| Base No. 4 | |
|---|---|
| Xanthan gum | 1.5 |
| Sodium alginate | 0.5 |
| Glycerin | 5.0 |
| Purified water | up to 100.0 |

| Base No. 5 | |
|---|---|
| Sodium alginate | 0.5 |
| Glycerin | 5.0 |
| Purified water | up to 100.0 |

| Base No. 6 | |
|---|---|
| Hydroxyethyl cellulose | 2.0 |
| Purified water | up to 100.0 |

Gel bases were prepared according to common technology at room temperature.[14] The bases with natural (xanthan, sodium alginate, and guar) and semi-synthetic (hydroxyethyl cellulose) gelators were prepared by the following method: At first the necessary amount of purified water was taken and the pre-prepared mixture of powders of the aforementioned gelators with glycerin was added by parts and stirred at medium revolutions of the mixer (40–60 r.p.m.) and left for some time (about an hour) for swelling and received semi-transparent gels (due to natural origin) with a specific scent of raw materials.

The base of the carbomer Ultrez 10 NF (gelator of synthetic origin) was prepared as follows: At first the necessary amount of purified water was taken, and then the required amount of this gelator and the chosen neutralizer were taken. The carbomer powder was sprayed over the surface of the water and allowed to dissolve for 30 min.

Then, a solution of alkali was added to neutralize the carbomer so that the whole surface of the solution was

treated and mixed until a transparent homogeneous gel was formed.

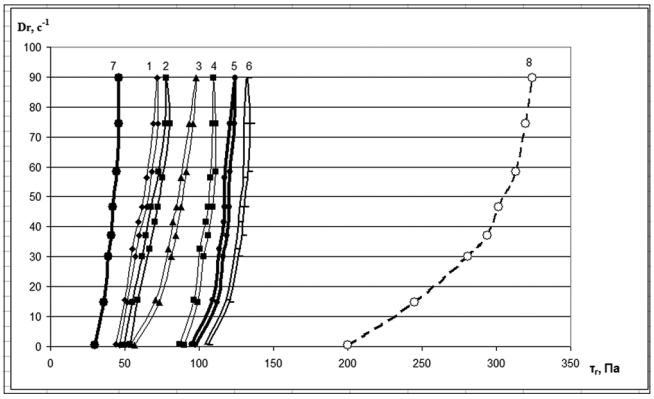


**Figure 1:** Rheograms, where: 7.8-rheological optimum, 1-6 - experimental samples

As a result of the technological studies, it was proved that the obtained gel bases had a non-Newtonian type of flow, plastic properties and practically instant thixotropy [Figure 1]. As we can see from Figure 1, all gel bases entered the rheological optimum, (reference to Polovka).

The next step was the introduction of fusidic acid into the prepared gel bases. Previously, we studied the solubility of fusidic acid. It has been experimentally determined that fusidic acid is soluble in ethanol (1:30), moderately soluble in glycerin (1:70) and is practically insoluble in water and sorbitol (70% solution).

Due to the impossibility of dissolving it in water, fusidic acid was pre-dissolved in alcoholic alcohol, and an alcoholic solution was added in the above-mentioned gel bases.

It is well-known that structural and mechanical properties of gel bases directly depend on the nature of origin (synthetic,

**Table 1:** Organoleptic and physical-chemical indicators of gel samples containing 2% fusidic acid

| Period of observation | Sample No. | Appearance of gel samples | Structural viscosity*, η (mPa • s) | MS | pH value | Colloidal stability |
|---|---|---|---|---|---|---|
| Freshly prepared samples | 1 | Gel mass of white color without odor | 6500 | 1.05 | 5.47±0.1 | Stable |
| | 2 | Gel transparent mass of pale yellow color without odor | 4700 | 1.54 | 5.23±0.1 | - |
| | 3 | Gel transparent mass of yellow color without odor | 3500 | 1.1 | 5.41±0.1 | - |
| | 4 | Gel transparent mass of pale yellow color without odor | 3200 | 1.17 | 5.46±0.1 | - |
| | 5 | Gel transparent mass of pale yellow color without odor | 3000 | 1.12 | 5.78±0.1 | - |
| | 6 | Gel mass of white color without odor | 3100 | 1.13 | 5.71±0.1 | - |
| 1.5 years later | 1 | Gel mass of white color without odor | 6480 | 1.05 | 5.47±0.1 | Stable |
| | 2 | Gel transparent mass of pale yellow color without odor | 4700 | 1.54 | 5.23±0.1 | - |
| | 3 | The sample split into layers | | | | |
| | 4 | Gel transparent mass of pale yellow color without odor | 3000 | 1.17 | 5.46±0.1 | - |
| | 5 | The sample split into layers | | | | |
| | 6 | The sample split into layers | | | | |
| 2 years and 3 months later | 1 | The sample split into layers | | | | |
| | 2 | Gel transparent mass of pale yellow color without odor | 1100 | 1.58 | 5.47±0.1 | - |
| | 4 | Gel transparent mass of pale yellow color without odor | 3410 | 1.08 | 5.46±0.1 | - |

natural) and on the properties of gelators ("strengthened compounds," solid gels and soft gels).[14,15]

At the given stage, the following indicators of the developed gel specimens were evaluated: Appearance, pH, structural viscosity (at 20 r.p.m.), and MS, colloidal stability. The samples were under observation for 2 years and 3 months at room temperature and in a cool place (reference DFU). Based on the performed research, the suggested shelf life is equal to 2 years.

It was proved that the pH values in all samples did not change over the entire observation period, and it was also noted that this interval was optimal for the agents for acne treatment.

Therefore, when studying the acne etiopathogenesis, it was noted that the development of microorganisms, in particular *Propionibacterium acne*, occurs in alkaline environment, which makes prospective the development of antimicrobial and anti-inflammatory agents with a pH value close to acidic.

As it can be seen from the data in Table 1, the structural viscosity decreased several times in the xanthan sample (No. 2) when 2 years and 3 months had passed, so this sample was excluded from the further research.

Sample No. 1 had satisfactory characteristics during the observation period, but the calculated MS values indicate a destruction of the gel + 2% fusidic acid system to certain degree in the mechanical process, thus this sample was excluded from further research.

1 years and 5 months later, the sample of gel No. 6 got split to layers and the active substance in samples of gels No. 1, 3, 5, i.e., −2% fusidic acid precipitated as white crystals.

On the basis of the data analysis Table 1. Sample No. 4 (based on a mixture of xanthan and sodium alginate) is optimal. It did not change its appearance during the entire period of observation and had satisfactory consumer properties.

The physical-chemical characteristics under study were also stable throughout the observation period, and that was the basis for their choice as carriers (bases) in the development of gel with 2% fusidic acid.

Thus, for further research, a gel sample with 2% fusidic acid and gel composition xanthan: Sodium alginate was selected.

## CONCLUSIONS

1. The structural-mechanical and physical-chemical properties of gel samples with 2% fusidic acid on the basis of promising gelators of different nature and origin: Hydroxyethyl cellulose, xanthan, sodium alginate, guar, and carbomer of the mark Ultrez-10 NF were studied.
2. The sample of gel based on a mixture of xanthan and sodium alginate was chosen, which was stable throughout the research period. This was confirmed by the determined index of MS (MS = 1.54–1.58) and the pH value (5.23–5.47).
3. It was shown that the gel with 2% fusidic acid based on a mixture of xanthan and sodium alginate is an elastic-viscoplastic system with practically instant thixotropic properties (that is typical of colloidal solutions) and satisfactory consumer characteristics.

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