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Comparison of the physical properties of ointments, creams and gels with ibuprofen obtained with two different methods according to the own compositions

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ABSTRACT

The aim of the study was preparing the skin formulations with ibuprofen as ointments, creams and gels. They have been prepared by two methods; melting the components and then mixing (method 1) and in the unqutor (method 2). The preparations have been tested rheologically and determined for the consistency, spreadability ex tempore and after 3 months of storage at 4°C. The studies showed that the consistency is stable during all the time of storage. The formulations prepared in the unquator have better consistency, spreadability and lower viscosity.

Keywords: ibuprofen, ointment, gel, cream, rheology, thixotropy

INTRODUCTION

Assessment of the physical properties is one of the most important criterion for determining the use of skin preparations. It is assumed that they have a significant influence on the way of application, stability and availability of the therapeutic substance from dosage form. Ibuprofen has anti-inflammatory and analgesic properties. It is used in the form of solutions, syrups, suspensions, capsules, tablets, ointments, emulsions, creams, gels, suppositories [1-4,6-9,14].

The preparations with ibuprofen for external use are easy to application and the side effects are marginal in comparison with preparations per os. The low penetration of ibuprofen across the stratum corneum of the skin requires the addition of the substances that improve the penetration and solubility. Nowadays, a lot of studies are conducted for developing the compositions of the most effective and non-toxic skin preparations [2,5,10-13].

That is why the aim of the study was comparison of the physical properties of ointments and gels with ibuprofen prepared according to our own recipe, using two different methods and determination of the influence of the method on the spreadability, viscosity and consistency.

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MATERIALS AND METHODS

Chemicals. Ibuprofen (acid form) – was received as the gift from IOL Chemicals and Pharmaceuticals Limited, Indie; White petrolatum – Galenic Laboratory, PZF „CEFARM– LUBLIN" S.A.; Lanolin – Galenic Laboratory, Olsztyn; Liquid paraffin – Galenic Laboratory, Olsztyn; SPEZIOL C 16 PHARMA (cethyl alcohol), SPEZIOL C 18 PHARMA (stearyl alcohol), SPEZIOL C 16-18 PHARMA (cethylstearyl alcohol), SPEZIOL V 95 G (sodium laurylsulphate), Lanette N PH (typ A: cetyl alcohol, sodium cetylsulphate), Lanette W PH (typ B: cetyl alcohol, sodium claurylsulphate), CUTINA GMS V PH (glycerol monostearate), POLYSORBATE 20 PH were received as the gift from Cognis, IMCD, Warsaw, Span 80 – Fluka Chemika, Switzerland, – MIGLYOL 812 – Chemische Werke Witten,Germany,- Methylocelulose – Aldrich, Germany, Syntalen MP was received as the gift from 3V SIGMA SPA, IMCD, Warsaw, Triethanoloamine P.P.H. POCh, Gliwice, Glicerol 86% – Galenic Laboratory, Olsztyn,- 1,2-Propylenoglykol – Laborchemie Apolda, Niemcy, Spirytus rectified – P.P.H. „STANLAB", Lublin, Metanol – P.P.H. „STANLAB", Lublin, Propylhydroxybenzoate (Saligin PP) was received as the gift from Salicylates and Chemicales PVT Ltd. Methylhydroxybenzoate (Saligin MP) was received as gift from Salicylates and Chemicales PVT Ltd.

Apparatus. Rheotest 2 Medingen viscometer (NRD); Extensometr (Department of Precision Mechanics in Lublin), Ultratermostat MLW UH 4 – VEB MLW Medingen Germany; Mixer Cito-UNGUATOR c/s – EPRUS, Magnetic stirrer – Typ MM 6.

PREPARATIONS

Preparations used to the studies had the character of ointments (PI – PIII), creams (PIV) and gels (PV-PVI). They were prepared by two methods: melting on the water bath (PI-PVI) and mixing in the unquator (PIu-PVIu).

Method1. Four ointment vehicles were prepared (PI-PIV). Solid and semisolid ingredients were melted and then after cooling, the liquid ingredients were added (Tab. 1).

Table 1. Composition of the preparations with ibuprofen

Components (g)	PI	PII	PIII	PIV	PV	PVI
Ibuprofen	2	2	2	2	2	2
White petrolatum	90	47.2	30	25	-	-
Lanolin	5.5	2.25	-	-	-	-
Liquid paraffin	-	-	35	-	10	
Gliceride	-	-	-	-	10	10
PPG-1,2	-	-	-	10	-	10
MC	-	-	-	-	2.5	-
Syntalen	-	-	-	-	-	1
Cutina	-	-	-	4.0	-	-
Speziol C16	0.5	-	30	-	-	-
Speziol C_{16-18}	-	9	-	-	-	-
Speziol V95	-	1	-	-	-	-
Lanettae WPH	-	-	-	6	-	-
Migylol 812	-	-	-	7.5	-	-
Tween 20	-	-	-	5.5	-	-
Span80	-	-	-	5.5	-	-
TEA	-	-	-	-	-	1.5
Saligin PP	0.1	0.1	0.1	0.1	0.1	0.1
Saligin MP	0.1	0.1	0.1	0.1	0.1	0.1
Ethanol (960g/l)	3	3	3	10	20	20
Water	-	35.25	-	28.5	55.5	55.5

Preparation V (PV) was prepared on the ground gel, dissolving methylcellulose in water at 70°C. After cooling, the other liquid substances were added to obtain the gruel and mixed.

Preparation VI (PVI) was prepared by dissolving Syntalen MP in the mixture of indicated solvents. The solution was neutralized by the addition of triethanolamine allowing gelation process.

After cooling of the ointment, vehicles and gels, the ethanol solution of ibuprofen was added. After solidification they were moved to the marked boxes (PI-PVI). Obtained preparations had the uniform color and consistency.

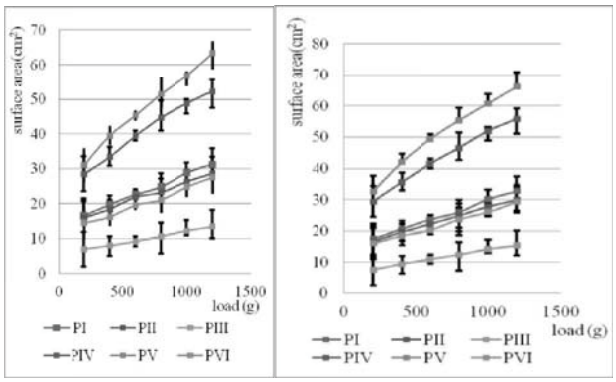
Method 2. The second part of preparation was made in the unquator by mixing solid and liquid components of the vehicle. In the end the ethanol solution of ibuprofen was added, mixed again to obtain the uniform consistency and moved to the marked boxes (PIu-PVIu). All preparations were stored at 4°C. The composition of the ointments and gels is given in Table 1.

INVESTIGATIONS

The determination of spreadability and viscosity of all preparations obtained with two methods was investigated.

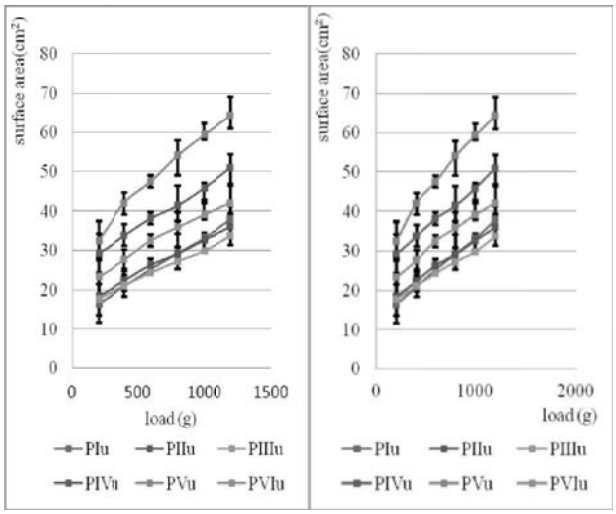
Determination of the spreadability

The spreadability was determined in the extensometer at 25±0.1°C. The relationship between the load and stretched surface of the preparation (cm^2) are showed on Fig. 1, 2.



a) extempore b) after three month

Fig. 1. The dependence between the load and the surface of the preparations



a) extempore b) after three month

Fig. 2. The dependence between the load and the surface of the preparations

Determination of the viscosity

Rheological studies were performed at 25°C and 32°C, using "RHEOTEST-2" with thermostat. The measurements were performed at shear rate Dr between 0.17-40 s^{-1}. The flow curves are showed on Fig. 3, 4, 5.

RESULTS AND DISCUSSION

All the preparations were white or cream, almost transparent. They were plastic and well spreadable on the skin. Their consistency was uniform and they have not di-

vided into layers. The preparations obtained in the unquator were softer than these ones obtained by traditional method.

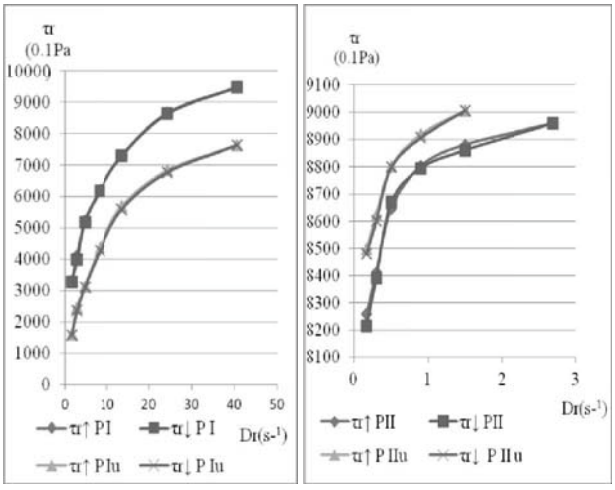


Fig. 3. Rheograms of preparations (PI, PIu, PII, PIIu) with ibuprofen

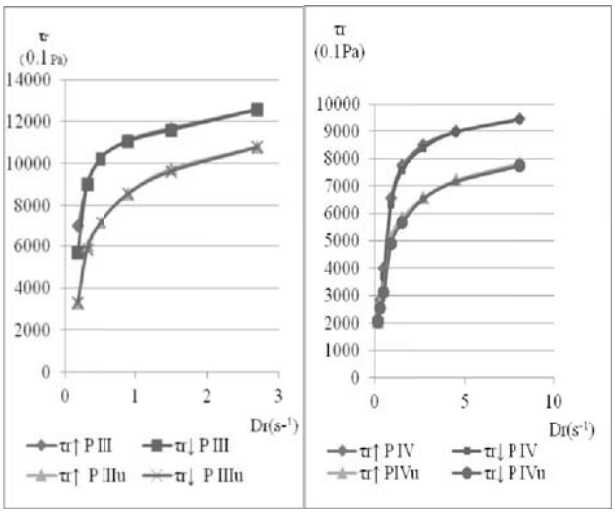


Fig. 4. Rheograms of preparations (PIII, PIIIu, PIV, PIV u) with ibuprofen

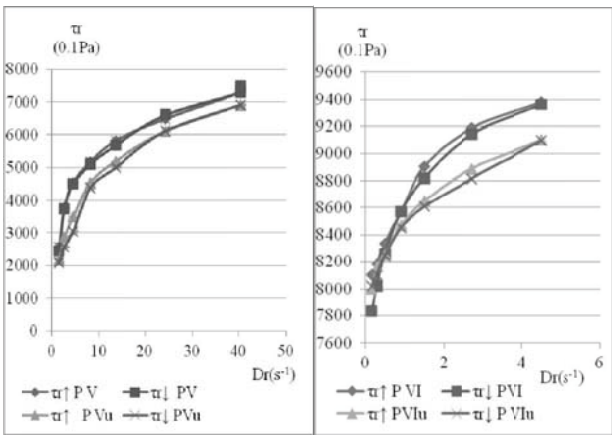


Fig. 5. Rheograms of preparations (PV,PVu,PVI,PVIu) with ibuprofen

Table 2. Viscosity parameters of preparations at shear rate to 2.7s^{-1}

Preparations	$\tau_r\uparrow$ [0.1 Pa]	$\eta\uparrow$ [mPa·s]	$\tau_r\downarrow$ [0.1 Pa]	$\eta\downarrow$ [mPa·s]
PI	4104	152000	3924	145333
PIu	2446	90592	2055	76111
PII	9218	341407	9198	340667
PIIu	8880	328889	8850	327778
PIII	12550	464815	12550	464815
PIIIu	10803	400111	10780	399259
PIV	8514	315333	8279	306630
PIVU	6582	243778	6329	234407
PV	3789	140333	3648	135111
PVu	2872	106370	2660	98518
PVI	9185	340185	9140	338518
PVIu	8885	329074	8815	326481

Figure 2 showed that preparations obtained in unquator (method 2) had better spreadability, except for the PIVu, where the spreadability was slightly smaller (about 2.4%). Much better spreadability was observed for the ointments prepared in unquator with Syntalen MP, PIIIu with cetyl alcohol and liquid paraffin.

The preparation PIII with addition of liquid paraffin and cetyl alcohol had the lowest spreadability. The spread surface of the preparations increased from 10% (PIII) to 50% (PI,PV). The addition of cetyl alcohol to lanoline and emulsifiers such as: Tween 20 and Span 80 significantly improved the spreadability of the preparations.

The spreadability of the studied preparations has not changed after one month of the storage at 4°C. The figures show that the spreadability increased from 4% to 13%.

The flow curves were performed as the dependence between shear stress ôr(0.1Pa) and shear rate Dr (s^{-1}) (Fig. 3, 4, 5). The course of the curves at 20°C indicates that all preparations have non-Newtonian character of flowing. The curves increase initially quite quickly at shear rate Dr (0.17-1.0 s^{-1}) in the preparations PII and PIIa, PIV and PIVu, PVI and PVIu ; at Dr (0.17- 0.5 s^{-1}) – PIII and PIIIu; at Dr (0.17-10.0 s^{-1}) – PV and PVu but then they move in straight lines. The shear stress has the slower nonlinear increase to the shear rate, thus the viscosity of these preparations decreases with the increase of shear rate.

At the chosen shear rate Dr = 2.7s^{-1} the viscosity of the preparations was compared. The preparation PIu had the lowest viscosity (90593 mPa· s), PVu - a little more higher (106370 mPa· s), PIII and PIIIu – the highest (464815 mPa· s and 400111 mPa· s) [Tab. 3].

The ointments and gels prepared by traditional method had higher values of viscosity than these mixed in the unquator. Moreover, the rheograms show the occurrence of phenomenon of thixotropy. The hysteresis loop areas were calculated under the ascending (H↑) and descending (H↓) curves and the difference between these areas. All the formulations showed the positive thixotropy. The preparations prepared in the unquator had the lower hysteresis loop areas, the ointment with vaseline, lanoline and cetyl alcohol – the biggest (PI: 2606 u.j., PIu: 2171 u.j.),

and for the ointments with addition of many emulsifiers and emulsifying vehicles PIV: 1779 u.j. and PIVu: 1605 u.j. The ointments PII and PIIu with cetostearyl alcohol, sodium laurylsulfateand 35.2% of water and PIII with liquid paraffin and cetyl alcohol had the lowest hysteresis loop areas (PII: 84 u.j., PIIu: 174 u.j., PIII: 174 u.j., PIIIu : 166 u.j.). Gels had similar, quite small magnitude of hysteresis loop areas [Tab. 3].

Table 3. Hysterezis loop areas obtained for the products PI-PVI i PIu-PVIu

Preparations	Surface area $H\uparrow$ (0.1 $Pa \cdot s^{-1}$)	Surface area $H\downarrow$ (0.1 $Pa \cdot s^{-1}$)	Hysteresis loop areas ΔH(0.1$Pa \cdot s^{-1}$)
PI	303950	301344	2606
PIu	233735	231564	2171
PII	22594	224834	110
PIIu	21584	21499	84
PIII	28589	28415	174
PIIIu	22894	22728	166
PIV	66140	64381	1757
PIVu	52869	51263	1605
PV	237543	237285	258
PVu	213050	212810	240
PVI	38894	38667	229
PVIu	37878	37714	165

CONCLUSIONS

1. All preparations have non-Newtonian flow character.
2. The composition and preparation method influences the consistency, spreadability and viscosity.
3. Gels have the best spreadability, the preparations with the addition of paraffin – the smallest. It can be the bioavailability criterion.
4. After 3 months of storage at 4°C there were no significant changes in the physicochemical properties of the preparations.

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