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N. A. Nagornaya, V. V. Gladyshev, B. S. Burlaka

Study of vinpocetine intranasal dosage form consistence properties

Zaporozhye State Medical University

Key words: *Vinpocetine, Intranasal Drug Administration, Rheology, «Mechanical Stability».*

Aim. Study of structural-mechanical nasal semisolid dosage forms on emulsion bases providing with optimal release active substance was done. Methods and results. Established vinpocetine nasal creams rheologic properties showed them as thixotropic systems. Restoration after stress removal is ceased by their structure coagulation bonds. Their consistent properties are completely situated within rheologic optimum of consistence limits.

Conclusion. Analysis of rheograms of flow allowed to reveal compositions of vinpocetine nasal emulsion ointments with optimal consistent properties and selected for the next preclinical investigations.

Вивчення консистентних властивостей інтраназальної лікарської форми вінпоцетину

Н. О. Нагорна, В. В. Гладышев, Б. С. Бурлака

Здійснили дослідження структурно-механічних інтраназальних м'яких лікарських форм вінпоцетину на емульсійних носіях, що забезпечують оптимальне вивільнення з них діючої речовини. Виявили, що реологічні властивості досліджених інтраназальних кремів вінпоцетину характеризують їх як тиксотропні системи, у структурі яких домінують коагуляційні зв'язки, які забезпечують їх повне відновлення після зняття напруження, і чий консистентні властивості знаходяться в межах оптимуму реології мазей. Аналіз реограм течії композицій дозволив встановити склади назальних емульсійних мазей із вінпоцетином, що мають оптимальні консистентні властивості й обрані для подальшого доклінічного вивчення.

Ключові слова: *вінпоцетин, інтраназальні препарати, реологія, «механічна стабільність».*

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Изучение консистентных свойств интраназальной лекарственной формы винпоцетина

Н. А. Нагорная, В. В. Гладышев, Б. С. Бурлака

Проведены исследования структурно-механических интраназальных мягких лекарственных форм винпоцетина на эмульсионных носителях, обеспечивающих оптимальную высвобождаемость из них действующего вещества. Установлено, что реологические свойства изученных интраназальных кремов винпоцетина характеризуют их как тиксотропные системы, в структуре которых доминируют коагуляционные связи, обеспечивающие их полное восстановление после снятия напряжений, и чьи консистентные свойства полностью находятся в пределах реологического оптимума мазей. Анализ реограмм течения композиций позволил установить составы назальных эмульсионных мазей с винпоцетином, обладающих оптимальными консистентными свойствами и отобранных для дальнейшего доклинического изучения.

Ключевые слова: *винпоцетин, интраназальные препараты, реология, «механическая стабильность».*

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Structural-mechanical characteristics of compositions have a marked influence on medicinal substances processes of releasing and absorption from the ointments and also on their consumer features: spreading, adhesion, capacity of squeezing out from the tubes [1,2,3].

Patient associates convenience and easiness of ointment applying on tissue or mucous membrane with efforts that are used to spread on the skin certain amount of ointment. That is similar to the process going on during movement of viscous and plastic material in the rotational viscosimeter, and patient's effort is a shear stress which characterizes resistibility of the materials to shear deformations by certain rate and can be measured instrumentally.

So the assessment of rheologic characteristics is an important and integral part of investigations in making of semisolid dosage forms for dermatological practice [5, 6].

As a result of complex physico-chemical, pharmacotechnological and biopharmaceutical investigations a formulation of nasal semisolid dosage form with vinpocetine – vasoactive biologically active substance which improves cerebral blood

circulation for angioneurologic practice was proposed by the department of Medicinal Preparations Technology of Zaporozhye State Medical University [7 - 9].

The aim of this work is study of consistent properties of developed ointment composition for treatment of cerebralvascular pathology.

Materials and methods

For the rheological investigations 0,5% vinpocetine ointments on emulsion bases providing with optimal releasing from the dosage form were used [10]. Formulations of vinpocetine nasal compositions are presented at *table 1*.

Study of structural-mechanical characteristics of compositions was carried out by the rotary viscosimeter «Reotest-2» with cylindrical arrangement. For the establishment of the consistent properties of system the sample of ointment composition was put in measurement device and then in thermostat during a half of an hour by the temperature 20°C. Then cylinder was rotated in measurement device by the twelve increasing in consecutive order shear rates, and readings of the indicated device were registered on each level. Destruction of studying system was carried out by the rotation of cylinder in measurement device in

Composition of intranasal ointment emulsion formulations with vinpocetine 0,5%

Table 1

Components	Bases (№№), %%		
	5	6	9
Vinpocetine	0,5	0,5	0,5
Glycerine		15	5
Twin 80	2	2	
Sunflower seed oil	15		15
Distilled monoglycerides	4	8	
Emulsifier №1	7,5		
Vaseline oil		20	
Emulsion wax		6	
Monostearate glycerine			5
Oleate-PEG-400			5
stearate-PEG-400			5
Ester II			3
Distilled water to	100	100	100

maximum rate during 10 minutes and after stopping of rotation on 10 minutes readings of the indicated device were registered on each of twelve decreasing rates. On the base of received results the value of maximum shear stress and efficient viscosity were calculated and rheograms of flow were drawn [11].

By the degree of structure permission of investigated systems in process of irreversible deformations it was judged using the value of «mechanical stability» which was calculated as ratio of strength limit before destruction to strength limit after destruction [12].

Results and discussion

Results of establishment dependence of efficient viscosity from shear rate for intranasal ointments with vinpocetine are presented at the *tab. 2-4* and they indicate presence of structure in gel systems because under the influence of increasing deformation forces their maximum shear stress is increased and efficient viscosity is decreased.

Table 2

Values of shear stress and efficient viscosity of intranasal ointment emulsion formulation with vinpocetine 0,5% №5

Shear rate, Dsec-№	Shear stress, (Pas)	Viscosity (Pas•sec)	Shear rate, Dsec-№	Shear stress (Pas)	Viscosity (Pas•sec)
3	86,67	28,89	1312	392,62	0,30
5,4	90,69	16,79	729	357,03	0,49
9	119,97	13,33	437,4	301,92	0,69
16,2	154,41	9,53	243	237,64	0,98
27	189,99	7,04	145,8	189,42	1,30
48,6	211,81	4,36	81	135,46	1,67
81	235,91	2,91	48,6	109,06	2,24
145,8	280,69	1,93	27	90,69	3,36
243	316,27	1,30	16,2	83,23	5,14
437,4	383,43	0,88	9	76,92	8,55
729	436,81	0,60	5,4	69,45	12,86
1312	460,35	0,35	3	66,01	22,00

Table 3

Values of shear stress and efficient viscosity of intranasal ointment emulsion formulation with vinpocetine 0,5% №6

Shear rate, Dsec-№	Shear stress, (Pas)	Viscosity (Pas•sec)	Shear rate, Dsec-№	Shear stress, (Pas)	Viscosity (Pas•sec)
3	82,08	27,36	1312	409,26	0,31
5,4	86,10	15,94	729	354,73	0,49
9	115,37	12,82	437,4	299,63	0,69
16,2	149,81	9,25	243	235,34	0,97
27	185,40	6,87	145,8	187,12	1,28
48,6	204,92	4,22	81	133,17	1,64
81	231,32	2,86	48,6	106,76	2,20
145,8	276,09	1,89	27	88,40	3,27
243	311,68	1,28	16,2	80,93	5,00
437,4	368,51	0,84	9	74,62	8,29
729	413,85	0,57	5,4	67,16	12,44
1312	455,76	0,35	3	63,71	21,24

Table 4

Values of shear stress and efficient viscosity of intranasal ointment emulsion formulation with vinpocetine 0,5% №9

Shear rate, Dsec-№	Shear stress, (Pas)	Viscosity (Pas•sec)	Shear rate, Dsec-№	Shear stress, (Pas)	Viscosity (Pas•sec)
3	110,78	36,93	1312	310,53	0,24
5,4	128,00	23,70	729	251,41	0,34
9	134,89	14,99	437,4	220,42	0,50
16,2	139,48	8,61	243	188,85	0,78
27	141,78	5,25	145,8	158,42	1,09
48,6	149,81	3,08	81	135,46	1,67
81	161,29	1,99	48,6	121,69	2,50
145,8	184,83	1,27	27	114,23	4,23
243	211,23	0,87	16,2	112,50	6,94
437,4	235,34	0,54	9	103,89	11,54
729	270,35	0,37	5,4	97,58	18,07
1312	321,44	0,25	3	90,69	30,23



Rheograms of flow of intranasal ointment emulsion formulations with vinpocetine are presented on fig. 1–3.

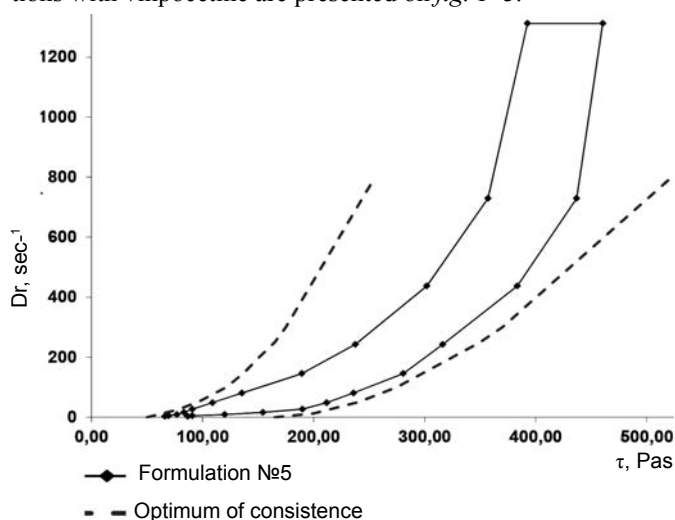


Fig. 1. Rheogram of intranasal ointment emulsion formulation with vinpocetine 0,5% №5.

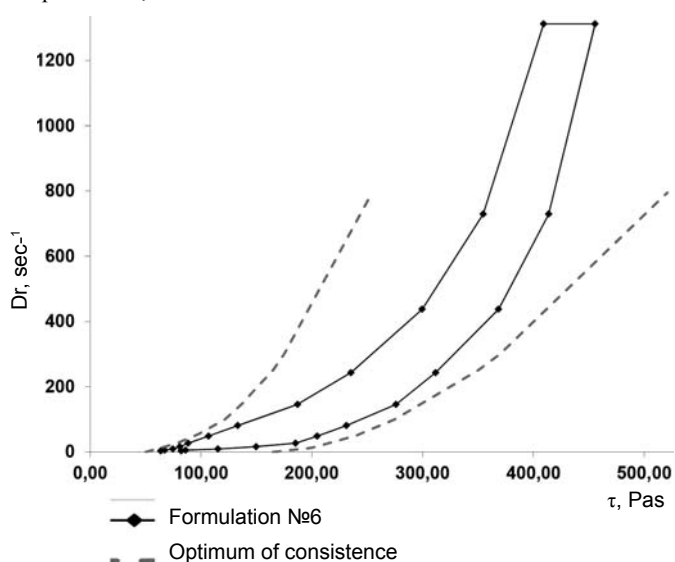


Fig. 2. Rheogram of intranasal ointment emulsion formulation with vinpocetine 0,5% №6.

Drown rheograms indicate that flow begins not instantly but after some applied stress necessary for the burst of structure elements. Tangent stress slowly increases with increasing of deformation rate to certain value. In period of again stress decreasing viscosity of investigating systems is restored permanently. That fact confirms the presence of plastic and viscous and thixotropic properties in intranasal ointment emulsion formulations with vinpocetine.

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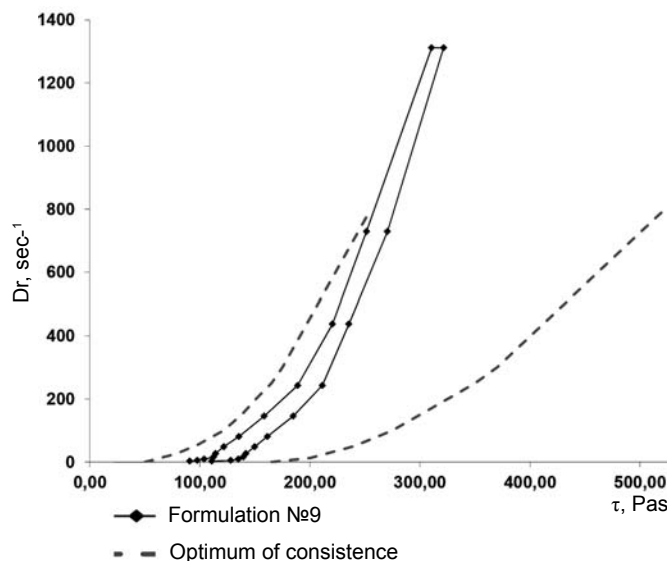


Fig. 3. Rheogram of intranasal ointment emulsion formulation with vinpocetine 0,5% №9.

It is significant that in period of again stress decreasing restoration of structure is permanently late. On the rheograms descending and ascending curves of all formulations form «hysteresis loop» with area for vinpocetine nasal ointments on the bases №5 and 6 much more larger than the same for base №9. That indicates bigger thixotropy and better consistent properties of their optimum of ointment consistence limits. Rheograms of all investigated vinpocetine intranasal dosage forms are completely situated within rheologic optimum of consistence limits [13].

Calculated «mechanical stability» vinpocetine nasal emulsion ointments on the bases №5 and 6 is 1,33.

It indicates that just coagulation bonds which provide with full deformation reversibility after removal of tension and keeping of rheological properties during long storing are presented in their structure [14].

Conclusion

1. Rheologic properties of the investigated vinpocetine nasal ointments on emulsion base characterize them as thixotropic systems and in their structure coagulation bonds prevail and ensure restoration after stress removal.

2. It was revealed that consistent properties of all investigated nasal systems are completely situated within rheologic optimum of consistence limits.

3. On the grounds of comparative estimation of rheological features for vinpocetine nasal semisolid dosage form and taking into account results of biopharmaceutical characteristics emulsion ointment №5 and №6 were offered to the next investigations.

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Information about authors:

Nagornaya N.A., post graduate student of Department of Medicinal Preparations Technology, Zaporizhzhya State Medical University.
Gladyshev V.V., head of Department of Medicinal Preparations Technology, Zaporizhzhya State Medical University, Professor, Doctor of pharmaceutical sciences, E-mail: gladyshev@v@gmail.com.
Burlaka B.S., Associate professor of Department of Medicinal Preparations Technology, Zaporizhzhya State Medical University, PhD.

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