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Biopharmaceutical Investigations of Microcapsulated Drug Formulation of Vinpocetine

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Abstract

In the experimental investigations using dispersion technique microcapsulated drug formulation of vinpocetine was obtained in a system «liquid-liquid». The process of release of the drug substance from microcapsules was studied in vitro in a dependence on the size of drug formulation, composition of the shell and dispersion medium where microcapsules were obtained. Optimal composition was selected for the elaborated drug formulation. Fused beeswax and cocoa butter in the ratio of 3:2 was found to be the most rational composition for the microcapsules with vinpocetine where the purified water and 2% solution of Na-CM cellulose was applied as dispersion medium.

Keywords: Biopharmaceutical Investigations, Microcapsulation, Vinpocetine

1. Introduction

In spite of certain successes in formation of the new medications for the treatment of neurological diseases accompanied by cerebral ischemia and disturbances of the mnestic functions a lot of the known pharmaceutical compositions (according to the data of multi-centered clinic investigations) though improving a neurological clinical outcome but does not reduce the death rate of the patients with these diseases[1,2].

An important role in complex therapy of the chronic cerebral circulatory disorder is concerned with the drugs improving cerebral circulation. One of the most widely applied medications is vinpocetine[1,3–5].

Vinpocetine has been shown to improve cerebral circulation and metabolism in the treatment of various types of cerebrovascular circulatory disorder, e.g. cerebral infarction, cerebral hemorrhage residual and cerebral arteries cirrhosis, etc. Due to its poor aqueous solubility and extensively metabolized during the first pass, its clinical use is greatly restricted by the low bioavailability after oral administration and so there is a need to improve its poor aqueous solubility to increase the oral bioavailability. An oral formulation with a high degree of oral absorption would, therefore, be highly desirable[6,7].

Presently, the most popular and needed drug formulation is a capsule, particularly, of a durable action which can also decrease the effect of humidity on stability of vinpocetine[8–10]. Additional microcapsulation of vinpocetine can to a considerable degree make a pharmacological effect of vinpocetine much more durable[11–14].

The aim of the work was to perform biopharmaceutical investigations concerning the choice of the optimal composition for the microcapsulated drug formulation of vinpocetine and to study the effect of shell compositions size of microcapsules on the release kinetics of vinpocetine from the elaborated drug formulation.

2. Materials and Methods

In the experiments vinpocetine [Figure 1] was used as an active pharmaceutical substance and additives registered for medical use and corresponding to the requirements of normative documents[1–21].

Microcapsulation was made by the usually applied in laboratories physical method - dispersion in the system liquid-liquid[14]. To obtain microcapsules by dispersion technique in immiscible liquids it is necessary to have two phases – hydrophilic and hydrophobic[15,16]. According to the references data from scientific literature the follow-

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ing ingredients are often used as a shell for microcapsules: Gelatin, beeswax and cocoa butter in different ratios[18,19]. When choosing composition of the melt – microcapsule shell in the process of the study the following ingredients were explored in the ratio of 3:2; and peach oil, purified water, petrolatum oil, solution of sodium - carboxymethyl cellulose 2% (Na-CM cellulose). As a result 4 model compositions of capsules were obtained.

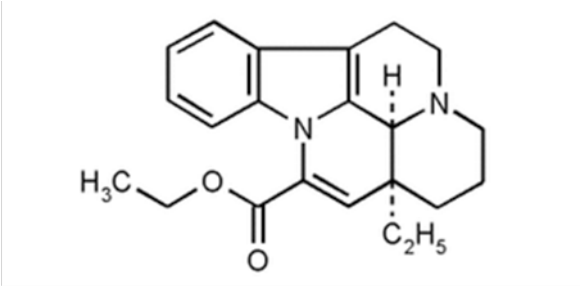

Figure 1. Structural formula of vinpocetine.

Compositions are presented in Table 1.

Table 1. Experimental compositions of microcapsules with vinpocetine

Composition, №	Constituent of microcapsule	Ingredients	Mass, г
1	Shell	Gelatin	10.0
		Purified water	25.0
	Core	Vinpocetine	0.05
	Dispersion medium	Vaseline oil	100.0
2	Shell	Gelatin	10.0
		Purified water	25.0
	Core	Vinpocetine	0.05
	Dispersion medium	Peach oil	100.0
3	Shell	Beeswax	12.0
		Cocoa butter	8.0
	Core	Vinpocetine	0.05
	Dispersion medium	Purified water	100.0
4	Shell	Beeswax	12.0
		Cocoa butter	8.0
	Core	Vinpocetine	0.05
	Dispersion medium	2% solution of Na-CM cellulose	100.0

Since microcapsulation implied retardation of the diffusion rate that can be regulated by the thickness of the shell and size of microcapsules themselves, according to the data known from the literature, the effect of these biopharmaceutical on the intensity of release of the pharmaceutical substance was studied in the work.

In order to make a comparative estimation of the degree of release for the reactant from the drug formulations a number of the authors performed biopharmaceutical investigations with the use of equilibrium dialysis through a semipermeable membrane. Cellophane film was applied as a membrane (thickness of 0.25 mm, size of the pores 50 μm), solvent medium used in the experiment was 95% ethanol. Microcapsules were separated into the fractions of 0.5-1.0 mm, 1-2 mm, 2-3 mm with the use of a set of sieves. Since vinpocetine is practically insoluble in water but well solved in ethanol, then ethyl alcohol was chosen as a dialysis medium. Sampling was made in 15, 30, 45, 60, 90 and 120 minutes. Release of the pharmaceutical substance was registered by spectrophotometric technique at the wavelength of 314 ±2 nm.

Kinetics of release of the pharmaceutical substance from microcapsules with the different shell (hydrophilic, hydrophobic) was studied as well as for the different sizes of microcapsules (0.5-1.0 mm, 1-2 mm, 2-3 mm).

3. Results and Discussion

Visually the obtained microcapsules represented small particles of yellow color, as a rule, with a round shape and size of 0.5 to 3 mm.

Figures 2-4 represent the plots showing the dependences of degree of release for the pharmaceutical substance into dialysis medium (%) on time (min.) [Figure 2, Figure 3 and Figure 4].

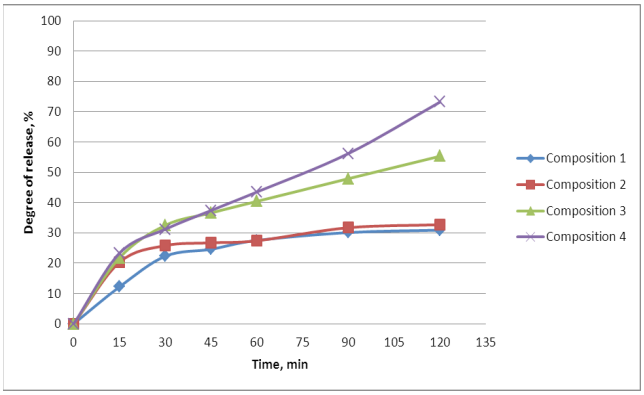

Figure 2. Dynamics of release for vinpocetine from microcapsules with a size of 0.5–1.0 mm.

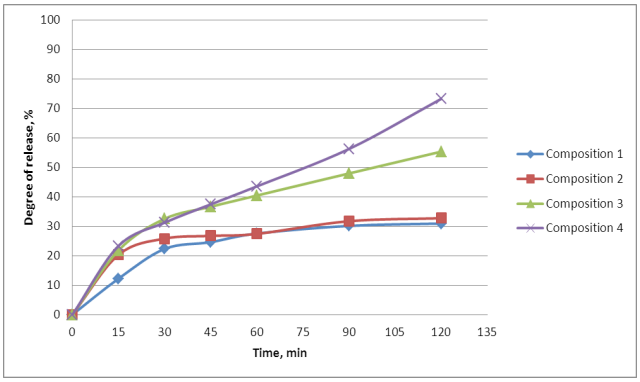

Figure 3. Dynamics of release for vinpocetine from microcapsules with a size of 1.0–2.0 mm.

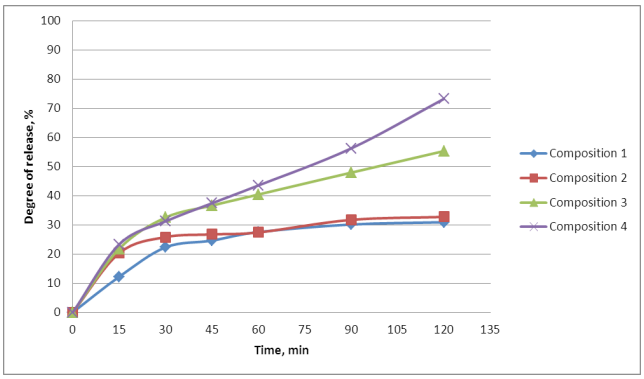

Figure 4. Dynamics of release for vinpocetine from microcapsules with a size of 2.0–3.0 mm.

As a result of the made biopharmaceutical investigations it was found that the release of vinpocetine from microcapsules into dialysis medium depends on their size, the nature of the shell and dialysis medium used in obtaining of microcapsules. So, the most complete and uniform relaease of the pharmaceutical substance takes place from microcapsules of all four compositions with a size of 0.5-1.0 mm. The most complete release of vinpocetine was observed for the microcapsules of composition number 4 and after 120 minutes from the start the degree of release attained 73.2% [Figure 5].

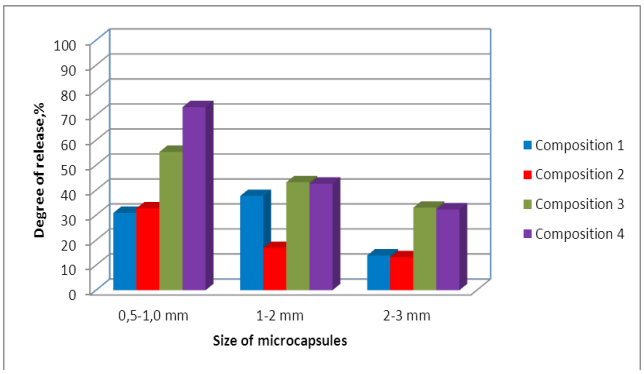

Figure 5. Results of vinpocetine release from the experimental compositions in a dependence of the size of microcapsules.

A considerable value on the rate of release of the pharmaceutical substance demonstrated dispersion medium where the microcapsules were obtained. Note, that for 120 minutes of the experiment more complete and uniform release from microcapsules of all the fractions with a composition 4 into dialysis medium was observed – up to 73.2% from the microcapsules with a size of 0.5-1 mm.

4. Conclusion

Thus, model samples of vinpocetine microcapsulues were obtained as a result of the performed investigations. It was found that the most complete release of the pharmaceutical substance took place from the microcapsules with hydrophobic coating, consisting of beeswax and cocoa butter in the ratio of 3:2, with a size of 0.5-1 mm. Dispersion medium for their producing was a 2% solution of Na-CM cellulose.

5. Acknowledgements

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