The evaluation of colloidal dispersions of PVA in the preparation of clonidine hydrochloride hydrophylic matrix tablets

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Introducere

The matrix-type formulations developed to obtain a sustained or prolonged release of active substances have been broadly studied in the past decades [1, 6].

Clonidine is a central α₂-adrenergic agonist that reduces blood pressure and slows heart rate by reducing sympathetic stimulation, used in the treatment of hypertension and in lower doses in the prophylaxis of migraine. The substance proves to be a suitable candidate in the formulation of tablets with a sustained release, due to the short half-life (two or three hours) [9].

PVA is a polymer who can be used in the preparation of hydrophylic matrixes. The polymer forms a gel through hydration, hence controlling the active substance release [1, 3, 6].

Having in view the technological criteria, developing an acceptable formula requires the presence of other excipients as the filler, the binder and the lubricant, besides the active substance and the matrix-former agent that can as well influence the release [6].

The purpose of the study was to prepare hydrophylic matrix tablets with clonidine basis and to asses the influence, that the type and the matrix-former agent ratio, as well as the presence of the filler and binder (granular lactose and starch and gelatine), have upon the release of clonidine.

Material and methods

- Clonidine hydrochloride, provided by Sicomed S.A., Romania;
- P.V.A. (polyvinylic alcohol with 88% hydrolysis degree) – Wego Chemical & Mineral Corporation;
- α-granular lactose – Meggle, Germany;
- Starch, magnesium stearate, talc and gelatine – import from Germany.

All substances used were certified for "pharmaceutical quality".

The preparation of the tablets

The tablets were obtained through the wet granulation and then by compression procedure of the clonidine hydrochloride and the selected excipients. Five formulations of the clonidine hydrochloride were produced by wet granulation with colloidal dispersions of PVA 10%, 15% and 20% in concentrations (Table 1). The wet-powder mass was then passed through an oscillating sieve (CISA – Spain) set a 50 rpm. The granules sieved were dried into a convection oven (Memmert, Germany) at 60°C for six hours, after which, they were re-screened using a 600-mesh sieve. The mixture was carried out in a cubic stirrer (Erweka, Germany) together the tableting excipients while...
the compression was made with an eccentric single punch tablet press (Korsch type).

<table>
<thead>
<tr>
<th>Components</th>
<th>Quantity [g]</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>F–1</td>
</tr>
<tr>
<td>Clonidine hydrochloride</td>
<td>0.0001</td>
</tr>
<tr>
<td>Colloidal dispersion of PVA 10% (900 cP)</td>
<td>0.1</td>
</tr>
<tr>
<td>Colloidal dispersion of PVA 15% (3000 cP)</td>
<td>-</td>
</tr>
<tr>
<td>Colloidal dispersion of PVA 20% (8200 cP)</td>
<td>-</td>
</tr>
<tr>
<td>Granular α-lactose</td>
<td>0.042</td>
</tr>
<tr>
<td>• Starch</td>
<td>0.0082</td>
</tr>
<tr>
<td>• Magnesium stearate</td>
<td></td>
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<tr>
<td>• Talc</td>
<td></td>
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<tr>
<td>• Gelatine</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>0.15</td>
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</tbody>
</table>

Table 1 – The formulations of the clonidine hydrochloride in the tablets

The study of clonidine hydrochloride dissolution from the hydrophylic matrix tablets

The dissolution test has been carried out in accordance with European Pharmacopoeia 2000 specifications. The determination was performed under the following conditions:

- Device no. 1: VanKel VK 7000 Dissolution Testing Station VanKel Technology Group, USA;
- Dissolution medium: distilled water;
- Medium volume: 900 mL;
- Temperature: 37 ± 0.5°C;
- Speed rotation: 75 rpm;
- Testing duration: eight hours.

The assays have been collected at predetermined time intervals (2, 4, 6, 8 hours).

The dosage has been performed under the conditions of the Romanian Pharmacopoeia Xth edition.

Results and discussions

The dynamics of the release of clonidine hydrochloride from the experimental hydrophylic matrices has been graphically represented (Figures 1–3).

The data analysis with regard to the substance release exhibits that several differences appear in the clonidine hydrochloride dissolution kinetics, because of the type and PVA ratio as well as of the amount of lactose and starch and gelatine present in the formulation. Therefore, it has been noticed that the highest degree of viscous PVA determines a slower release, in comparison to other types of polymers with a lower viscosity.

In all cases, the substance release is made gradually, and, especially, in the case of F–2 formula (within PVA as matrix former is 10% in concentration per tablet mass), the dissolute percentage of the substance provided in the specified time intervals, complies with the standards in force.

It has also been noticed that the nature of the filler/binder excipient influences the release profile from the pharmaceutical form. In this case, the differences may be the result of the solubility
and the different binding capacity of the two excipients.

Conclusions

In accordance with the study results, it has been drawn the conclusion that PVA determines a sustained release of the clonidine hydrochloride, which, is dependent on its viscosity degree and the ratio being used.

The lactose association in the formulations (soluble filler) increases the release speed compared to the PVA (filler – strong binder).

Choosing the appropriate type and concentration of the polymer (PVA), as well as the right nature of the filler and binder, may lead to the modeling of the clonidine hydrochloride kinetics release in order to produce hydrophobic matrix tablets with a sustained substance release.

Bibliografie

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