Influence of pH in swelling capacity and dissolution profiles of budesonide formulated in tablets of a novel hidrogel

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Synthesis of the hydrogel

This work presents the synthesis of a novel poly(magnesium acrylate) hydrogel called PAMgA, developed for oral drug delivery systems. The hydrogel has a concentration of 5 mM of cross-linker agent, ammonium persulfate (PSA), that confers long segments between linking points in magnesium acrylate monomer chains (AMgA).

The synthesis of the hydrogel is carried out in two stages:

- Synthesis of the magnesium acrylate monomers (AMgA)
- Polymerization reaction to obtain the hydrogel PAMgA

a) Synthesis of AMgA

The preparation of the monomer AMgA is carried out by a neutralization reaction. Two mol of acrylic acid are added dropwise to a solution of magnesium hydroxide, under constant stirring. When the dispersion becomes transparent, the end of the reaction is reached.

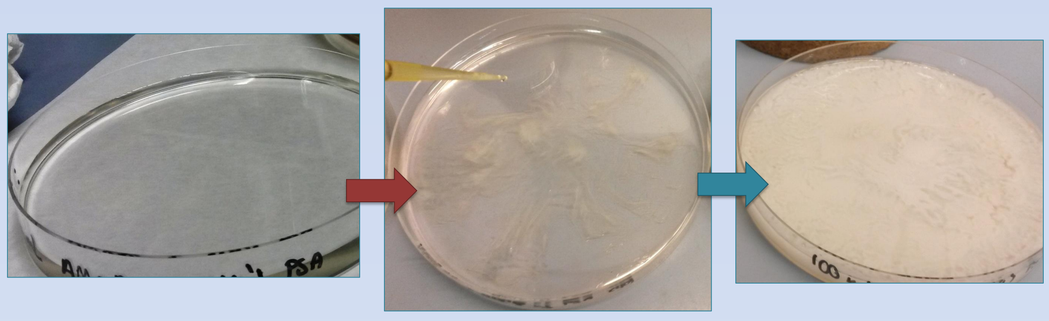
The pH is adjusted to neutral and the solution of the monomer formed is filtered. Finally, the monomer AMgA is concentrated at 25 wt.% in a rotator evaporator.

In this stage, care must be taken with the increase in temperature, to avoid spontaneous polymerization of the monomer.

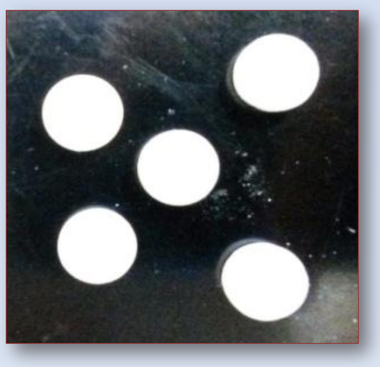
b) Synthesis of PAMgA

The synthesis of poly(magnesium acrylate) is carried out by the free radical polymerization method, using ammonium persulfate (PSA) as iniciator and TEMED as a catalyst.

PSA was used at a concentration of 5mM. This low concentration of PSA provides an hydrogel with long chains of acrylic acid, which are able to capture water in its structure. Once the reaction is finished, the polymer formed is washed during 7 days with distilled water. This step is essential to guarantee that any rest of monomer is eliminated. Finally the hydrogel is freeze-dried.



Tablets elaboration



White, biconcave and brilliant PAMgA-tablets containing a dose of 9 mg of budesonide are obtained. The average weight is of 191 ± 4,15 mg, the diameter of 8,10 ± 0,02 cm and the hardness of 61 ± 1,5

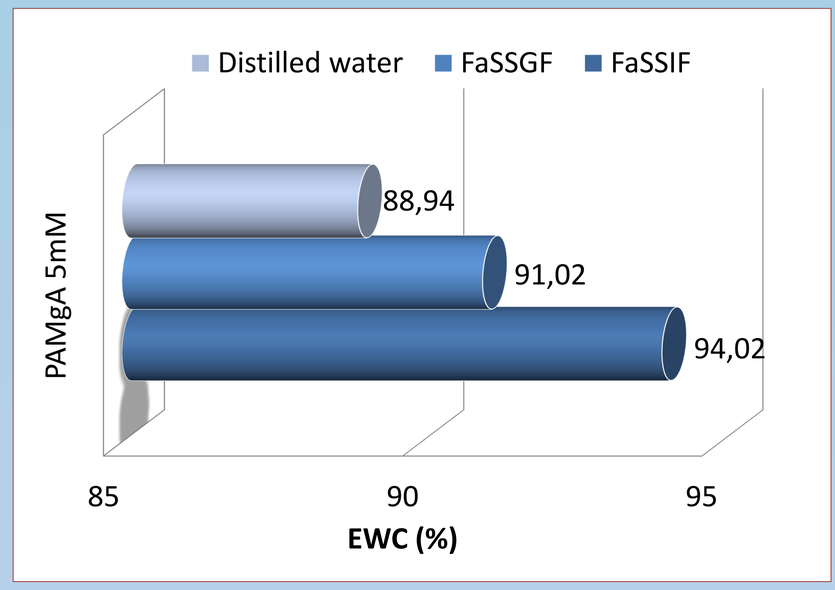
Swelling Capacity

The swelling capacity is determined by the gravimetric method. Tablets with PAMgA are elaborated, and placed in beakers with 3 different media: distilled water, simulated gastric fluid at pH 1,2 (FaSSGF) and simulated intestinal fluid at pH 6,8 (FaSSIF).

The percentage equilibrium water content (EWC) is calculated with the ecuation:

$$EWC = \frac{W_F - W_O}{W_F} \times 100$$

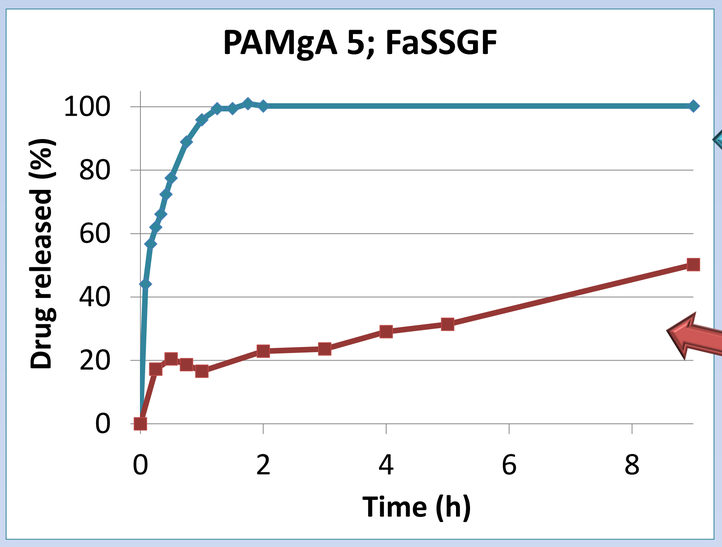
where Wf refers to the weight of the tablet at equilibrium and Wo is the dry weight of the tablet (before the assay).



The EWC calculated is slightly higher at pH 6,8 (94,02 ± 0,03%) than al pH 1,2 (91,02 ± 0,05%) and than in water (88,94 ± 0,03%), may be due to the interaction of the ions with the polymer chains.

Drug Dissolution

Due to the low solubility of the active ingredient in aqueous medium, 0,5% of sodium lauryl sulfate (SLS) is added to both biorrelevant media: FaSSGF and FaSSIF, in order to guarantee sink conditions during the dissolution assay.

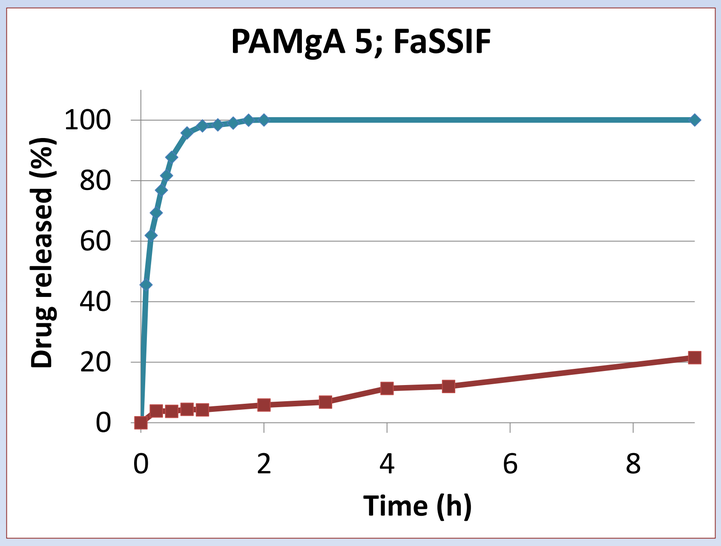


Budesonide as powder

Tablets containing 9 mg of budesonide

Budesonide, as raw material, is totally dissolved in 1 hour in both dissolution media.

Budesonide contained in the tablets shows a very low dissolution rate (lower at pH 6,8), although the 100% of the drug is released after 24 hours in both media.



Conclusions

The new PAMgA hydrogel synthetised is shown as a good excipient for sustained drug delivery devices for oral administration, because of Its good compresibility and its swelling capability that controls drug release in contact to aqueous media .

Bibliography

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