ORIGINAL ARTICLE

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pH-Sensitive Soy Protein Films For The Controlled Release Of An Anti-Inflammatory Drug

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Executive Summary

pH-responsive delivery systems based on biodegradable polymers represent one of the most rapidly advancing areas of science. Such delivery systems offer numerous advantages compared to conventional dosage forms including improved efficacy, localized delivery of the drug to a particular part of the body, improved patient compliance, and convenience [1]. However, only a reduced number of biodegradable drug delivery systems exhibiting such behavior are known [2, 3, 4]. Proteins present, by nature, interesting characteristics to be used in the production of this type of systems since their total net charge varies with pH. In this study, the possibility of producing water-based, pH-responsive soy protein films with an encapsulated model drug (meclofenamic acid-sodium salt, MFASS) was explored.

Glyoxal crosslinked and non-crosslinked MFASS-encapsulated soy films were prepared by solvent-casting and evaluated for their in vitro degradation and release behavior.
The release of MFASS from the soy films was found to be dependent on the pH of the immersion solution. The different films studied were immersed at 37 °C in three isotonic saline solutions buffered at different pH: 5, 7.4, and 10 (Fig.2). Negligible drug release occurred at pH 5 due to the low drug solubility and a zero net charge of soy. However, over a 97% release was observed after 240 h and 29 h of immersion at pH 7.4 and pH 10, respectively. These differences may be attributed to both protein chemistry (negative net charges) and high drug solubility at those pHs.

The release of MFASS from the soy films was affected, to a certain extent, by the respective degree of crosslinking (Fig. 3). Regardless OF the amount of glyoxal used, the release from crosslinked films was 15% slower than that from the non-crosslinked ones. At pH 7.4, total release (>97%) occurred at 336 h for crosslinked films, in contrast with the 240 h necessary for the total release from non-crosslinked ones.
The MFASS release data was processed according to the Higuchi model (up to 60% release) [25]. The good fitting of the release kinetics with the model indicated that the drug release was mainly diffusion-governed.
Based on the provided methodology, desirable pH-sensitive soy protein films might be easily manufactured and used for the release of drugs in response to pH changes in the application site.

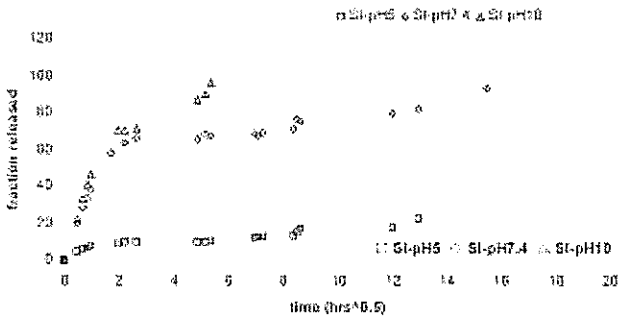

Fig. 2. Release of meclofenamic acid-sodium salt (MFASS) vs. square root of time from soy film (SI) after immersion, at 37 °C, in an isotonic saline buffer media of pH 5 (□), 7.4 (◇) and 10 (△). S.D.s were within ±0.05 in all cases

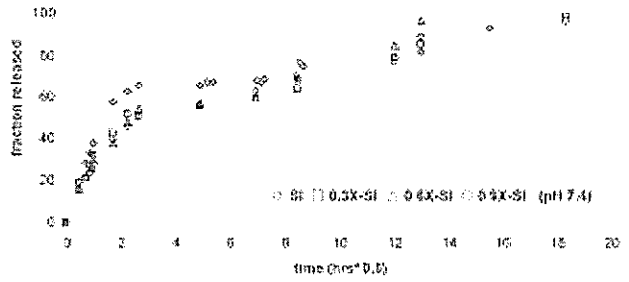

Fig. 3. Release of meclofenamic acid-sodium salt (MFASS) vs. square root of time from soy films Non-crosslinked (SI ◇), crosslinked with 0.3% glyoxal (0.3X-SI □), crosslinked with 0.6% glyoxal (0.6X-SI △) and crosslinked with 0.9% glyoxal (0.9X-SI ○) after immersion, at 37 °C, in an isotonic saline buffer media of pH 7.4. S.D.s were within ±0.12 in all cases

Keywords *Soy protein Film-casting Drug release Glyoxal crosslinking pH-sensitive Mechanical properties Higuchi model Degradation*

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