Preparation and Evaluation of Diclofenac Sodium–Cellulose Acetate Microcapsules Using Solvent Evaporation Technique

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Abstract

- The aim of this work is the preparation of diclofenac sodium microcapsules using cellulose acetate as a polymer by solvent evaporation technique. Two emulsifiers, namely polyvinyl alcohol and sodium lauryl sulfate were employed. The prepared microcapsules were evaluated for their morphology and surface structure, average particle size, yield, drug loading efficiency, and their release pattern. The release of diclofenac sodium from cellulose acetate microcapsules was pH dependent. The drug was released faster in the alkaline medium compared to acidic medium.

Introduction

- The emulsion solvent evaporation technique has been widely used for the formulation of different drugs into microcapsules using various polymeric materials . This technique is simple and factors affecting microcapsule size distribution and drug release are easily modified . Our work was undertaken to prepare sustained release diclofenac sodium microcapsules, by solvent evaporation technique, using cellulose acetate. The variables affecting the microencapsulation process, namely, polymer concentration, organic solvent composition and emulsifier type and concentration were extensively studied, in a trial to optimize the yield, loading efficiency and release characteristics of the produced microcapsules. We also investigated the effect of dissolution media pH on the in vitro release.

Design of the experiment

* Microcapsules prepared using polyvinyl alcohol (PVA)

Polyvinyl alcohol was used as aqueous phase emulsifier, and the influence of the following formulation variables were studied: a) The aqueous phase volume (distilled water): 120 and 240 ml. b) The organic phase volume (methylene chloride : acetone 3:2) 30, 50, 80 ml. c) Drug: Polymer ratio 1: 1, 1: 2. d) Polyvinyl alcohol concentration 0.5, 1.0, 2.0% (w/v).

•Microcapsules prepared using sodium lauryl sulfate (SDS)

•Sodium lanryl sulfate was used as emulsifier, and microcapsules were prepared following the formulation parameters that were proven to be optimum in case of PVA. Hence 120 ml distilled water was used as an external phase and 50 ml as an internal phase at D : P ratio of 1:1 and 1:2 using either. a) SDS in two different concentrations 0.5 and 1%. b) Mixture of 0.5% SDS and 0.5% PVA.

Preparation of cellulose acetate Microcapsules

The microcapsules were prepared by solvent evaporation method in 250 ml beaker, using a mechanical stirrer at 400 rpm. The calculated amount of the polymer cellulose acetate (CA) was dissolved in the specified volume of methylene chloride and acetone followed by dissolving the calculated amount of the drug (DS) to form the internal phase. The external phase was prepared by dissolving the specific amount of the emulsifier in 120 ml distilled water. The internal phase was added drop wise to the external phase, using a 20 ml syringe at a rate of 0.5 ml/min. After complete addition of the internal phase, methylene chloride – acetone mixture was allowed to evaporate. The microcapsules were collected by filteration, washed with distilled water, left to dry at ambient conditions for 24 hrs and stored in a desiccator until used.

RESULTS AND DISCUSSION

Particle diameters and Production yield determination

Table (1,2) Particle diameters (um)of diclofenac sodium- cellulose acetate microcapsules.

D : P ratio	Methylene chloride-acetone mixture volume	Microcapsule Diameter (μm) Polyvinyl alcohol concentration (%) 0.5	1.0	2.0
1:1	30 ml	182.33	156.62	141.71
	50 ml	162.60	139.41	112.31
1:2	30 ml	262.31	191.42	169.9
	50 ml	273.61	176.9	147.6

D : P ratio	Methylene chloride-acetone mixture volume	Yield Polyvinyl alcohol concentration 0.5	2.0	2.0
1:1	30 ml	96.3	89.4	83
	50 ml	97.1	91.3	84
1:2	30 ml	92.5	86.4	79.9
	50 ml	91.0	86.1	80.3

Figure(1): Production yield curves at (a) 30 ml methylene chloride- acetone mixture (b) 50 ml mixture.

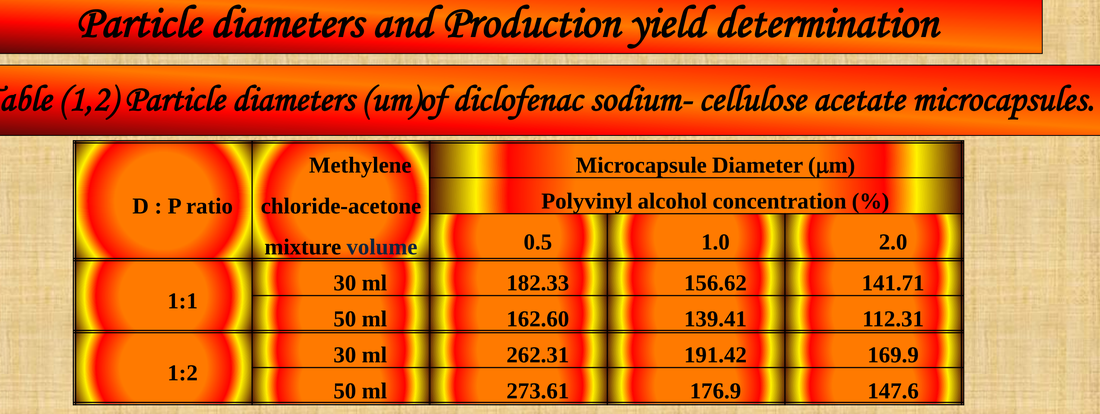


Table (3) Loading efficiency values of different diclofenac sodium microcapsules

D : P ratio	1:1						1:2					
Methylene chloride-acetone volume (ml)	30			50			30			50		
PVA concentration (%)	0.5%	1%	2%	0.5%	1%	2%	0.5%	1%	2%	0.5%	1%	2%
Theoretical drug loading (%)	50	50	50	50	50	50	33.33	33.33	33.33	33.33	33.33	33.33
Actual drug loading (%)	38.5	37.3	36.9	46.8	44.7	42.3	24.8	23.3	22.5	28.7	27.9	26.8
Loading efficiency (%) mean+SD	77±2.9	74.6±3.7	73.8±2.8	93.6±4.2	89.6±3.7	84.6±3.5	74.4±2.5	69.9±2.8	67.5±4.2	86.1±2.9	83.7±3.7	80.4±3.7

Photo-microsopic determination of diclofenac sodium cellulose acetate microparticles

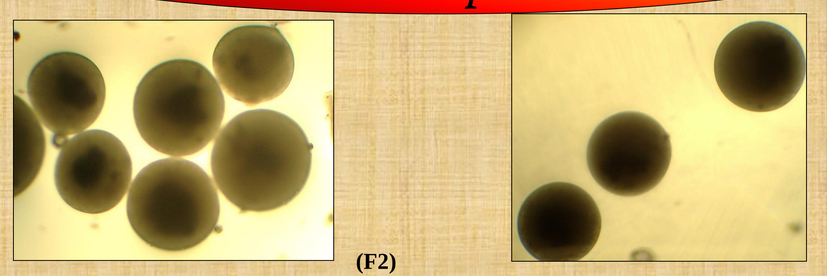
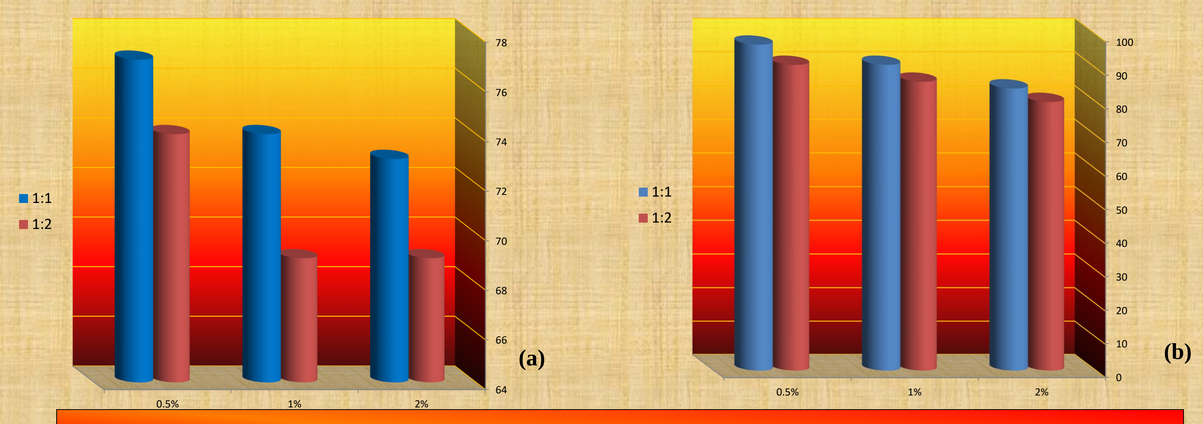


Figure (2): Optical micrograph of diclofenac sodium- sodium cellulose acetate microparticles,F2,F6.

Figure(3): Loading efficiency curves at (a) 30 ml methylene chloride- acetone mixture (b) 50 ml mixture.



•In-vitro release and kinetic studies of diclofenac sodium capsules

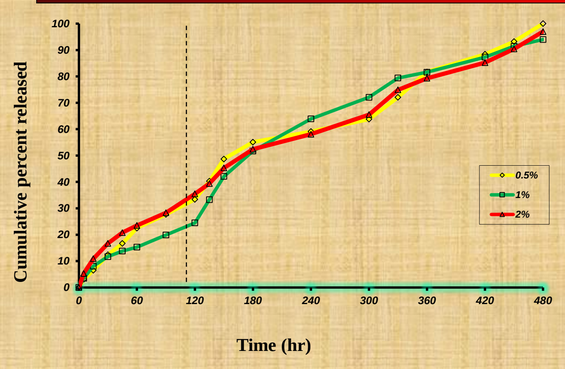


Figure (4): Release of diclofenac sodium-cellulose acetate capsules using drug : polymer ratio 1:1 and 30 ml solvent.

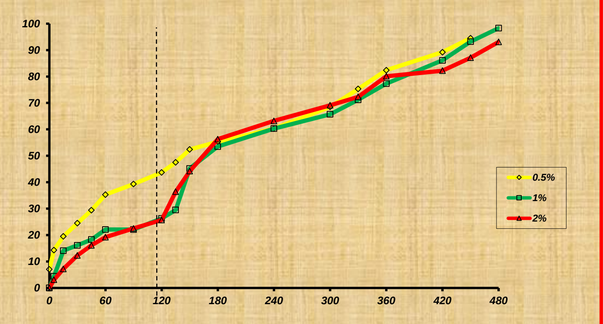


Figure (5): Release of diclofenac sodium-cellulose acetate capsules using drug : polymer ratio 1:1 and 50 ml solvent.

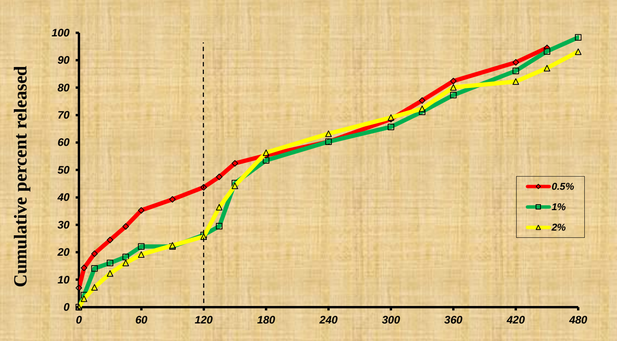


Figure (6): Release of diclofenac sodium-cellulose acetate capsules using drug : polymer ratio 1:2and 30 ml solvent.

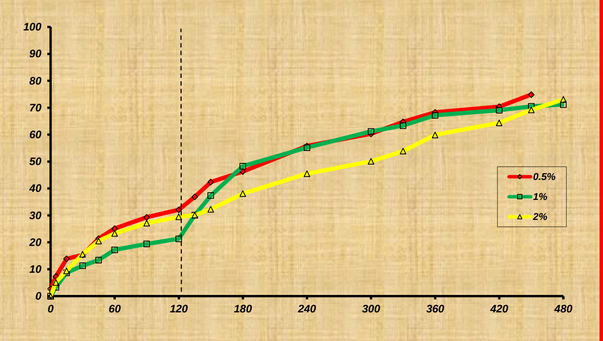


Figure (7): Release of diclofenac sodium-cellulose acetate capsules using drug : polymer ratio 1:2and 30 ml solvent.

Table (4): Microencapsulation parameters of diclofenac sodium-cellulose acetate microcapsules prepared using 0.5% sodium lauryl sulfate + 0.5% polyvinyl alcohol.

Microencapsulation parameters	Drug to polymer ratio 1:1	1:2
Microcapsule diameter (μm)	194.7	252.5
Microcapsule yield (%)	93.6	88.4
Theoretical drug loading (%)	50.0	33.33
Actual drug loading (%)	41.53	22.3
Loading efficiency (%) (mean ± SD)	83.06±3.54	66.9±4.41

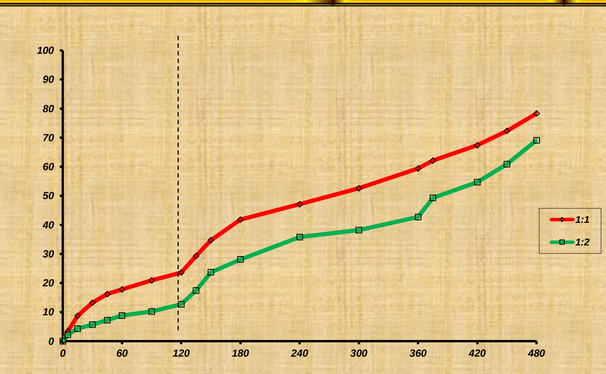


Figure (8): Release profile of diclofenac sodium-cellulose acetate microcapsules prepared using 0.5% sodium lauryl sulfate + 0.5% polyvinyl alcohol and 50 ml methylene chloride- acetone mixture.

Conclusion

Diclofenac sodium–cellulose acetate microcapsules were successfully prepared applying the solvent evaporation technique. Changing the polymer content does not effect the morphology of the produced microcapsules. Drug to polymer ratios of 1:1 and 1:2 produced discrete, spherical and freely flowing micro-capsules. The increase in the polymer amount increased the mean particle size and decreased the yield of the microcapsule due to the increase in the internal phase viscosity. The microcapsule shell remained intact after exposure to thedissolution medium and the drug was released by passage through the microcapsules surface pores. The release of diclofenac sodium from cellulose acetate microcapsules was pH dependent. The drug was released faster in the alkaline medium compared to acidic medium.