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Formulation and Evaluation of Metronidazole Loaded Cross Linked Sodium Alginate and Xanthum Gum Microspheres

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ABSTRACT
Metronidazole-loaded microspheres, formulated with sodium alginate and xanthan gum via ionotropic gelation, were developed and evaluated for controlled drug delivery. Varying polymer ratios and crosslinking agent concentrations yielded microspheres characterized for size, entrapment efficiency, swelling, morphology, and in vitro release. FTIR and DSC confirmed drug-polymer compatibility. Spherical morphology with smooth surfaces was observed via SEM. Polymer blend ratios significantly influenced drug release, achieving sustained release over 12 hours. Formulation F4 (1:1 polymer ratio, optimized crosslinking) exhibited the highest entrapment (87.5%) and sustained release, suggesting crosslinked sodium alginate/xanthan gum microspheres as a promising system for controlled metronidazole delivery.

KEYWORDS: Metronidazole, Microspheres, Sodium alginate, Xanthan gum,Natural polymers, Mucoadhesive microspheres

I. INTRODUCTION

Harnessing the biocompatibility of natural polymers, this study investigates metronidazole-loaded microspheres formulated with sodium alginate and xanthan gum via ionotropic gelation. This approach aims to achieve controlled drug release, enhancing bioavailability and reducing dosing frequency—critical improvements for this widely used antimicrobial agent. The resulting microspheres were characterized to evaluate their potential as an effective controlled delivery system.

II. LITERATURE REVIEW

The utility of natural polymers, such as sodium alginate and xanthan gum, in formulating controlled drug delivery systems via microspheres is well-established (Jain N.K. et al., 2008; Chatterjee S. et al., 2017). These polymers offer biocompatibility and the potential to modulate drug release. Studies have indicated that combining alginate and xanthan gum can provide beneficial properties, including efficient drug encapsulation and controlled release rates (Chatterjee S. et al., 2017; Roy H. et al., 2011). Prior research has specifically explored metronidazole-loaded alginate microspheres prepared using ionic gelation, demonstrating sustained drug release influenced by polymer and crosslinker concentrations (Alalor CA et al., 2018; Das M.K. and Das S.K,2011)

III. AIM AND OBJECTIVE

This study aimed to formulate and evaluate crosslinked sodium alginate and xanthan gum microspheres for the controlled delivery of metronidazole. The objectives encompassed: (1) preparing metronidazole-loaded microspheres using these polymers with various crosslinking agents; (2) characterizing the physicochemical properties of the resulting microspheres, including particle size, yield, swelling index, and drug entrapment efficiency; and (3) assessing their in vitro drug release profile and release kinetics

IV. MATERIALS USED

Metronidazole-loaded microspheres were formulated using a modified ionotropic gelation method. Briefly, a homogeneous solution of sodium alginate and xanthan gum in purified water, containing dissolved metronidazole, was prepared. This solution was then extruded dropwise through a flat-tipped needle into gently stirred aqueous solutions of different crosslinking agents: 1% w/v maleic anhydride (F1), 1% w/v aluminium chloride (F2), and 1% w/v barium chloride (F3). The formed microspheres were allowed to cure in the respective crosslinking solutions for 15 minutes to achieve spherical shape and structural integrity.Subsequently, the microspheres were separated by filtration using a mesh strainer and washed thoroughly with distilled water to remove any unreacted crosslinking agent. Finally, the washed microspheres were spread on Petri dishes

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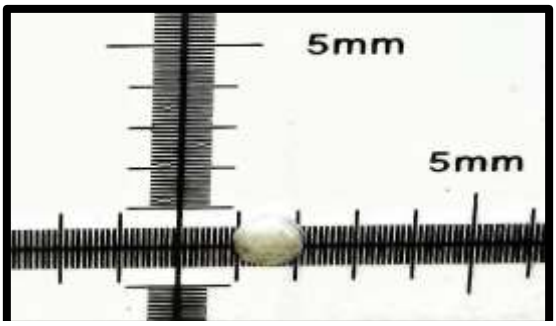
and dried at ambient room temperature until a constant weight was achieved.

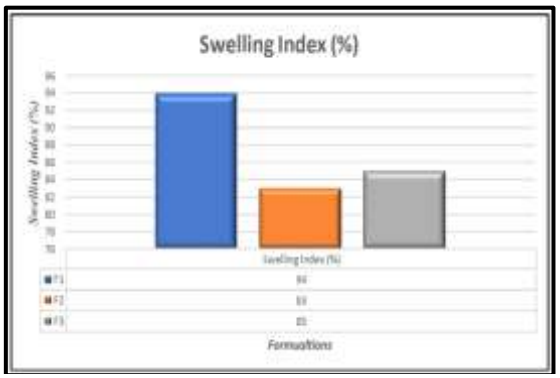
V. METHODS

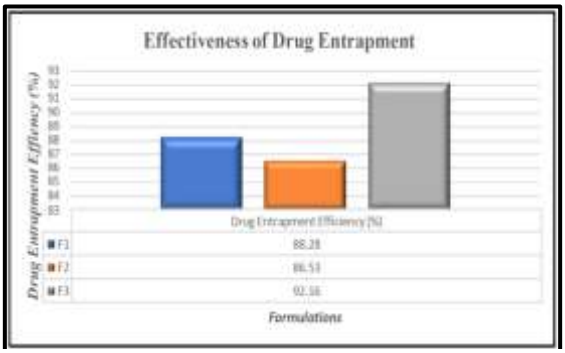
The dried microspheres were then subjected to various evaluation parameters. Particle size was determined using a digital microscope by measuring the diameter of several randomly selected microspheres. The percentage yield of each formulation was calculated by comparing the weight of the dried microspheres to the initial weight of the drug and polymers. The swelling index was assessed by immersing a known weight of microspheres in distilled water for one hour and measuring the increase in weight. Drug entrapment efficiency was determined by crushing a known weight of microspheres, dissolving them in water, and quantifying the metronidazole content using a UV-Vis spectrophotometer at a predetermined wavelength. In vitro drug release studies were conducted using a USP Type II dissolution apparatus with distilled water as the dissolution medium, maintained at 37 ± 0.5°C and stirred at 50 rpm. Samples were withdrawn at predetermined time intervals, and the amount of metronidazole released was quantified using UV-Vis spectrophotometry. The resulting release data were fitted to various kinetic models (zero-order, first-order, Higuchi, Hixson-Crowell, and Korsmeyer-Peppas) to determine the drug release mechanism. Drug-polymer compatibility was confirmed using FTIR and DSC analyses, while the surface morphology of the microspheres was examined using scanning electron microscopy (SEM).

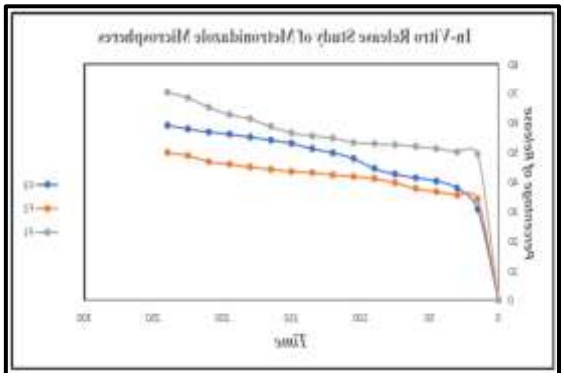
VI. RESULT AND DISCUSSION

Metronidazole-loaded microspheres were successfully prepared using sodium alginate and xanthan gum with three different crosslinking agents (F1: maleic anhydride, F2: aluminium chloride, F3: barium chloride). Particle size analysis revealed average diameters of 1.1 mm, 1.2 mm, and 0.9 mm for F1, F2, and F3, respectively. Formulation F3 exhibited the highest percentage yield (89.62%) and drug entrapment efficiency (92.16%), suggesting barium chloride facilitated more efficient microsphere formation and drug incorporation. Swelling index values indicated varying water uptake capacities, with F1 showing the highest swelling (94%).









In vitro release studies demonstrated sustained drug release over 240 minutes for all formulations (Figure 3.7). Formulation F1 exhibited the fastest release (70.47%), while F2 (50.05%) and F3 (59.26%) showed comparatively

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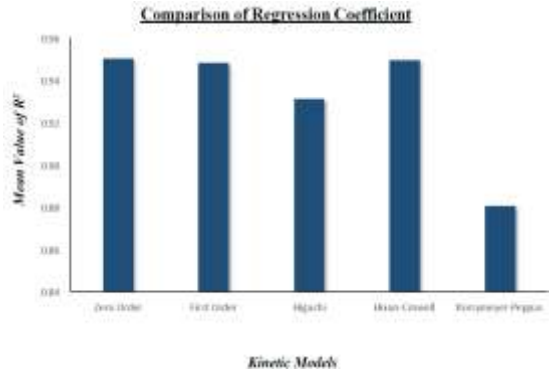
slower release rates. Kinetic modelling revealed that drug release from F1 best fit the zero-order model (R^2 = 0.9211), indicating a near constant release rate, possibly due to its higher swelling and less dense matrix. Conversely, F2 and F3 release profiles were best described by the Higuchi model (R^2 = 0.9819 and 0.9875, respectively), suggesting a diffusion-controlled mechanism through a more rigid matrix formed by aluminium and barium chloride crosslinking. These findings highlight the significant influence of the crosslinking agent on the physicochemical properties and drug release characteristics of the sodium alginate-xanthan gum microspheres, with potential implications for tailoring drug delivery for specific therapeutic applications.



VII. CONCLUSIONS

In conclusion, this study successfully formulated metronidazole-loaded microspheres utilizing the biocompatible natural polymers sodium alginate and xanthan gum through the straightforward ionic gelation technique. The choice of crosslinking agent (maleic anhydride, aluminium chloride, or barium chloride) significantly influenced the physicochemical characteristics of the resulting microspheres, including particle size, yield, and drug entrapment efficiency, with barium chloride crosslinked microspheres (F3) demonstrating superior drug incorporation. In vitro release studies revealed sustained drug release over a 240-minute period for all formulations, albeit with distinct kinetic profiles. Formulation F1 exhibited a release pattern approaching zero-order kinetics, potentially advantageous for maintaining constant drug levels, while F2 and F3 demonstrated release governed by diffusion, as evidenced by their fit to the Higuchi model. These findings underscore the potential of tailoring the drug release characteristics of sodium alginate-xanthan gum microspheres for metronidazole delivery by carefully selecting the crosslinking agent, offering a promising avenue for developing improved therapeutic formulations.

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