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FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLET OF PECTIN IN COMBINATION WITH OTHER HYDROPHILIC POLYMER

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Abstract *Physico-chemical characteristics of pectin and guar gum were found to be within the specified limits. The guar gum showed passable compressibility index, high % of swelling and passable angle of repose as compared to pectin. Swelling and erosion experiment were carried out with tablets containing different ratios of guar to pectin using USP 24 Type II apparatus. From the result it was observed that guar gum has greater swelling capacity and pectin has high erosion rate. In-vitro drug release from the formulation batch F_3 and F_{4s} was found to be most promising and show optimum release in a controlled manner for 10 h. The formulation batch F_4 shows the zero-order release. At the same polymer level (pectin and guar gum). The effect of different filler excipients were studied (batch F_3). It was observed that tablets prepared with lactose shows faster release and recompress decrease the drug release from diltiazem HCl matrix tablets. All the formulation batches tested for physical parameters like weight variation, hardness, friability and drug content, all were found to be within the I. P. limits. The in-vitro drug release data showed that the optimized formulation batch F_3 follows the Korsmeyer-peppas model, indicating that the possible mechanism of drug release was by non-Fickian diffusion. The optimized formulation batch F_4 follows the zero order release. The drug-excipient interaction studies were carried out by FTIR and DSC. No significant interaction of drug with polymer was observed. During stability studies, no significant variation (1 to 3%) in drug release was observed, indicating that formulation batch F_3 and F_4 were stable over the chosen condition for 2 months. The optimized formulation batch F_3 and F_4 showed better drug release profile with Dilzem SR (diltiazem HCL , Torrent) and Voveran SR (diclofenac sodium ,Novartis) respectively. This was concluded from the similarity factor (f_2), which was found to be 53.53 and 52.40 respectively.*

Keywords *Pectin , sustained release, Polymer, Formulation*

INTRODUCTION

SUSTAINED RELEASE DOSAGE FORMS

The aim of any drug delivery system is to provide therapeutic amount of drug to appropriate site in the body to achieve immediate therapeutic response and to maintain the desired drug concentration. In the recent years sustained release (SR) dosage forms continue to draw attention in the research for improved patient compliance and decreased incidence of adverse drug rections.[1]Sustained release technology is relatively new field and as a consequence, research in this field has been extremely fertile and has produced many discoveries. New and more sophisticated controlled release/sustained release delivery system are constantly being developed and tested. Advantage of a controlled or sustained drug delivery system over a conventional dosage forms are[3]:

[1] Improved patient convenience and compliance due to less frequent administration.
[2] Reduction in fluctuations in steady state levels and therefore better control of disease condition and reduced intensity of local or systemic side effects.
[3] Increased safety margin of high potency drugs due to better control of plasma levels.
[4] Maximum utilization of drug enabling reduction in total amount of dose administered.

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[5] Reduction in health care costs through improved therapy, shorter treatment period, less frequency of dosing, reduction in personnel time to dispense administer and monitor patients.

OBJECTIVE

[1] An immediately available dose to establish the blood level quickly in an amount sufficient to produce the desired Pharmacological response i.e. (Loading dose).

[2] The remaining amount of total dose (maintenance dose) is then gradually released to maintain constant blood level of the drug.

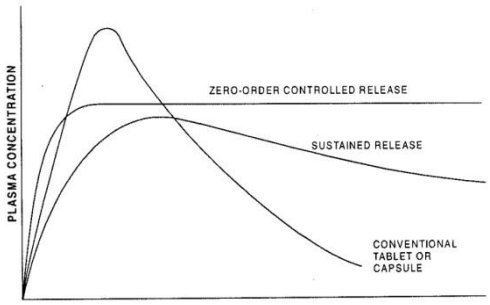

Figure 1.1: Plasma drug concentration profiles for conventional tablet or capsule formulation, a sustained release formulation and a zero order controlled release formulation.

MAIN OBJECTIVE AND PLAN OF WORK

1. The main objective of this work was to use pectin (HM) in combination with guar gum that control the burst effect by promoting gelation (radial-axial expansion) and also to examine the release mechanism for guar-pectin combination matrix system.

2. Objective of present investigation was to formulate and evaluate a sustained release tablet of high methoxylated pectin in combination with other hydrophilic polymer using water soluble and sparingly soluble drug as a model.

PLAN OF WORK

To achieve this objective, the following plan of work was envisaged.

[1] Physical characterization of pectin and guar gum

- Total ash value
- Acid insoluble matter
- Loss on drying
- Test for presence of salmonellae typhi
- Determination of pH
- Determination of viscosity
- Determination of percentage water uptake
- Study of physical parameters : color, odor, texture, mesh
- Solubility behavior
- Micrometrical study: angle of repose, bulk density, tapped density and percentage compressibility.
- Effect of pH on solubility
- Swelling study
- IR spectroscopy characterization

[2] Preparation and evaluation of sustained release matrix tablet using pectin.

- Weight variation
- Friability
- Hardness
- Content of active ingredient
- *In-vitro* dissolution study

[3] Preparation and evaluation of sustained release tablet using different ratios of pectin and guar gum.

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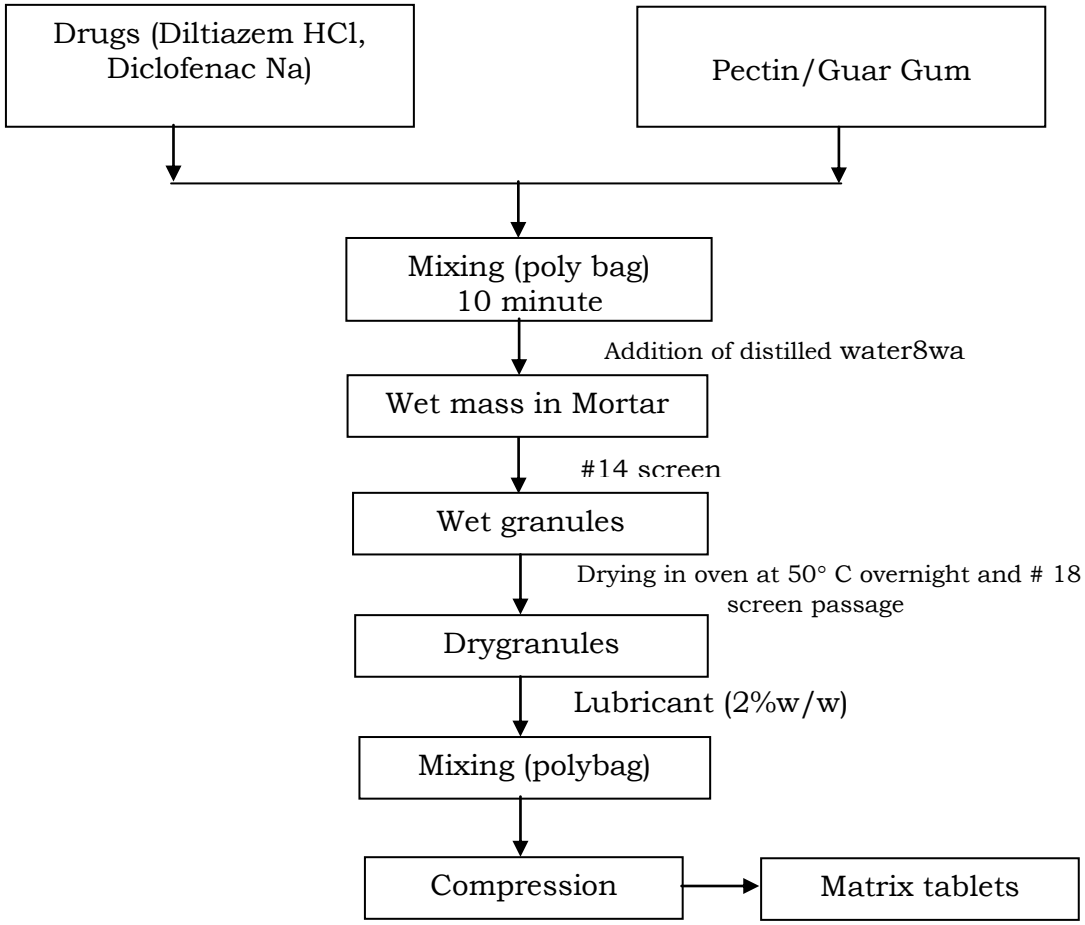
- Weight variation
- Friability
- Hardness
- Content of active ingredient
- *In-vitro* dissolution study

[4] Study the effect of different fillers on SR matrix tablet
- MCC (Avicel pH 101)
- Lactose
- DCP (Emcompress®)Starch

[5] Drug excipients compatibility studies
- DSC studies
- FTIR studies

[6] Stability study of the final selected formulation.

[7] Comparison with marketed formulation.



RESULT AND DISCUSSION

Review of the literature on polymers strongly indicates that, the polymers from natural origin are finding an increasing range of application in pharmaceutical research and dosage form design.

With this background, combination of guar gum and pectin were selected as a matrix forming material for sustained release (SR) tablet formulation. Because when guar matrix tablet is exposed to the dissolution medium, the guar interact slowly with water and does not gel rapidly and also initial burst effect is observed. Whereas, addition of pectin to guar appears to modulate and promote gelation (radial-axial expansions) which might provide controlled rate of drug release.

Physico-chemical characteristics of pectin and guar gum were found to be within the specified limits. The guar gum showed passable compressibility index, high % of swelling and passable angle

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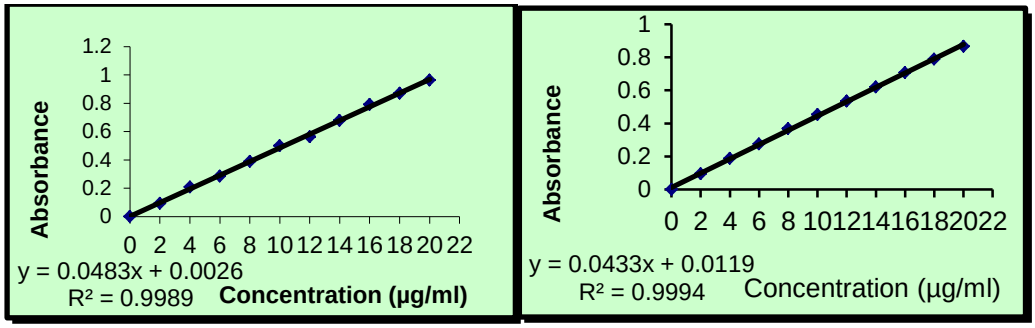
of repose as compared to pectin.

Swelling and erosion experiment were carried out with tablets containing different ratios of guar to pectin using USP 24 Type II apparatus. From the result it was observed that guar gum has greater swelling capacity and pectin has high erosion rate.

In-vitro drug release from the formulation batch F_3 and F_{4s} was found to be most promising and show optimum release in a controlled manner for 10 h. The formulation batch F_4 shows the zero-order release.

At the same polymer level (pectin and guar gum). The effect of different filler excipients were studied (batch F_3). It was observed that tablets prepared with lactose shows faster release and emcompress decrease the drug release from diltiazemHCl matrix tablets.



STANDARD CALIBRATION CURVE FOR DILTIAZEM HCL IN DISTILLED WATER

- All the formulation batches tested for physical parameters like weight variation, hardness, friability and drug content, all were found to be within the I. P. limits.

CALIBRATION CURVE

- The in-vitro drug release data showed that the optimized formulation batch F_3 follows the Korsmeyer-peppas model, indicating that the possible mechanism of drug release was by non-Fickian diffusion. The optimized formulation batch F_4 follows the zero order release.
- The drug-excipient interaction studies were carried out by FTIR and DSC. No significant interaction of drug with polymer was observed.
- During stability studies, no significant variation (1 to 3%) in drug release was observed, indicating that formulation batch F_3 and F_4 were stable over the chosen condition for 2 months.
- The optimized formulation batch F_3 and F_4 showed better drug release profile with Dilzem SR (diltiazem HCL , Torrent) and Voveran SR (diclofenac sodium ,Novartis) respectively. This was concluded from the similarity factor (f_2), which was found to be 53.53 and 52.40 respectively.

CONCLUSION

[1] DiltiazemHCl sustained release matrix tablets was successfully formulated by using the combination of pectin (HM) and guar gum in the ratio of 1:2 (Drug: polymer).

[2] Zero order release of diclofenac sodium was achieved by combination of guar gum and pectin (HM) in the ratio 1:0.5 [Drug: polymer].

[3] Combination of guar gum and pectin (HM) is an interesting polymer mixture for the preparation of SR matrix tablet because of high water swellability, non toxicity and low cost of guar gum and good binding and gelling capacity of pectin.

[4] Swelling and erosion experiment concluded that the % swelling was in the order guar >pectin-guar>pectin and % erosion rate was in the order pectin>pectin-guar>guar gum.

[5] All the formulation batches fulfill the I. P. limit for physical parameters like weight variation, hardness, friability and drug content uniformity.

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[6] The in-vitro drug release studies indicated that the optimum release profile was found by formulation batch F3 and F4.
[7] At the same polymer level, the in-vitro drug release decreased in the order of lactose, starch, MCC and emcompress® as filler excipients (batch F3).
[8] By drug-excipient interaction studies, no significant interaction was found.
[9] Formulation batch F3 and F4 were found to be stable over the chosen temperature and humidity for two months.
[10] Formulation batch F3 has better SR profile as compared to marketed product.

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