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Formulation and Evaluation of Clarithromycin Extended Release Tablets

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Abstract
The Present study to investigate the formulation development of orally administrable Clarithromycin delayed release tablet. Clarithromycin tablet was designed for the delaying the release to prolong the duration of drug action with the help of various polymers like Microcrystalline Cellulose, HPMC K4M, HPMC K5M, HPMC 6CPS, PEG 6000 with different additives are used for the trial and error method. The prepared tablets shown good dissolution data. The preliminary results from this study suggest that tablets prepared from MCC, HPMC 6CPS and PEG 6000 can be used to incorporate antibiotics like Clarithromycin and may be effective when administered orally in the stomach against *H. pylori*.
Key words: Clarithromycin, HPMC 6CPS, Extended Release Tablets,

Introduction

H. pylori is a small, spiral, gram negative organism which colonizes on gastric mucosa of human stomach and produces a serious gastro duodenal disease—including peptic ulcers, gastric lymphoma and acute chronic gastritis[1]. Although *H.pylori* is highly sensitive to most antibiotics, its eradication from patients requires high concentration of drugs to be maintained within the gastric mucous for a longer duration. Thus it can be expected that local delivery of narrow spectrum antibiotics through a site-specific or gastro-retentive drug delivery system may result in complete removal of the organisms in the fungal area of the gastric mucosa due to bactericidal drug levels being attained in the area, and might lead to better treatment of peptic ulcer disease[2].

One way to bring out the complete eradication of *H. pylori* is to treat with one or more antibiotics combined with an anti-secretory agent but these regimens are not fully effective because of patient compliance, side effects and bacterial resistance problems [3]. Other than the multi-antibiotic therapy, different therapeutic strategies have been examined to completely eradicate *H. pylori* from the stomach [4, 5].

Another way to enhance the eradication rate of *H. pylori* is to extend the residence time of the antibiotics in the stomach. The longer residence time of dosage forms will allow more of the antibiotic to penetrate through the gastric mucus layer to act on *H. pylori* where *H. pylori* exists thereby improve the therapeutic efficacy. Moreover, the absorption of an antibiotic into the mucus through the mucus layer (from the gastric lumen) is believed to be more effective for *H. pylori* eradication than absorption through the basolateral membrane [3, 6].

Clarithromycin is a macrolide, orally absorbed, broad spectrum antibiotic. It is widely used in a standard eradication treatment of gastric *H. pylori* infection combined with a second antibiotic and an acid-suppressing agent [4, 7].

Materials and Methods

Materials:

Clarithromycin was received as gift sample from Cipla Pharma Pvt Limited, Vapi India. Microcrystalline Cellulose (MCC), Sodium Dihydrogen Phosphate Di Hydrate, HPMC K4M, HPMC K5M, HPMC 6CPS, PEG 6000 were purchased. All other chemicals were of analytical grade.

Methods:

Preparation of Clarithromycin Tablets: The various batches of tablet formulations were prepared by wet granulation method. Clarithromycin was mixed with different concentration of Polymers (MCC, HPMC K4M, HPMC K5M HPMC 6CPS, PEG 6000) were used for the different batches. The binding agent was added to the above mixture. The wet mass is passed through sieve # 10 and dried at 60°C for 20 minutes. The dried granules were passed through sieve # 20 then lubricated with talc and magnesium stearate. The granules were then compressed using Rotary Tablet Machine to obtain the tablets.

Evaluation of Formulation:

Physical Characters: The tablets were analyzed for weight variation test (n=20), hardness (n 6), (Monsanto hardness tester), thickness (n=5) using a vernier caliper and friability (Roche Friabilator).

Content Uniformity Test: The formulated Tablets were subjected to content uniformity test was performed by following the assay procedure as per the USP 24.

In-vitro dissolution study: The Clarithromycin release rate was performed by using USP dissolution test apparatus Type II (paddle method) using 900 ml of 0.IN HCI at 37 ± 0.5°C at 50 rpm. This study was done for 24 hrs. A sample of 5 ml were withdrawn at an interval of l5min,30min,lhr,2hr,4hr, 8hr, l2hr, l6hr, 20hr and 24hr respectively. The samples were replaced with fresh dissolution medium each time. The samples were filtered through 0.45trn membrane filter. Samples were suitably diluted with 2ml of F. C. Phenol Reagent (diluted to 1:2 with distilled water) and 2rn1 of 20 % sodium carbonate solution and the volume made up to 10 ml with dissolution media. The resultant samples were analyzed at 760 nm against reagent blank.

Results and Discussion

The prepared tablets of different formulations were evaluated for the weight variation test, thickness and hardness. The weight variation, thickness and hardness values showed no significant difference from the average value. The friability was also within the specified limits. The drug content in all the formulations of Clarithromycin tablets was within the range of 95 to 105%. This ensured good uniformity of the drug content in the tablets.
To study the effect of Release study Initial trials were used with the HPMC K4M, HPMC K5M, with HPMC 6CPS were used concentration was varied from 14 to 20% approximately. The optimal concentration i.e. 17% was found to be satisfactory shown in table 1. Increasing the concentration of the HPMC K4M resulted in the decrease in the release of Clarithromycin and increase in the tablet. Eventhough these initial trials (CDF1-CDF3) release rate were not satisfactory, further it was decided to change the microcrystalline cellulose with HPMC K4M, HPMC K5M. Trial Formulation (CDF4 –CDF 6) tablets were shown the release of linearity with prolonged time for 24hrs was found to be successful than the trial formulations (CDF1-CDF3) with HPMC K4M, HPMC K5M. Among the formulation (CDF4 –CDF 6) tablets decrease in MCC concentration the final part of the 24hrs release was insufficient or short, The Optimal concentration of MCC around 20% was found to effective and linear release was found which shown in Fig 1. The repeatability of trials where shown the reproducibility of the successful formulations of

Table 1: Formulations of Carithromycin Delayed Release Tablets

Content/ Formulation Code	CDF 1 (mg)	CDF 2 (mg)	CDF 3 (mg)	CDF 4 (mg)	CDF 5 (mg)	CDF 6 (mg)
Carithromycin (Per Tablet)	500	500	500	500	500	500
Microcrystalline Cellulose(MCC)				125	150	175
Sodium Dihydrogen Phosphate Di Hydrate	65	65	65	65	65	65
HPMC K4M	50	25	25			
HPMC K5M	50	25	25			
HPMC 6CPS	25	50	50	50	25	25
PEG 6000	25	25	25	25	25	25
Talc	5	5	5	5	5	5
Magnesium Sterate	2.5	2.5	2.5	2.5	2.5	2.5

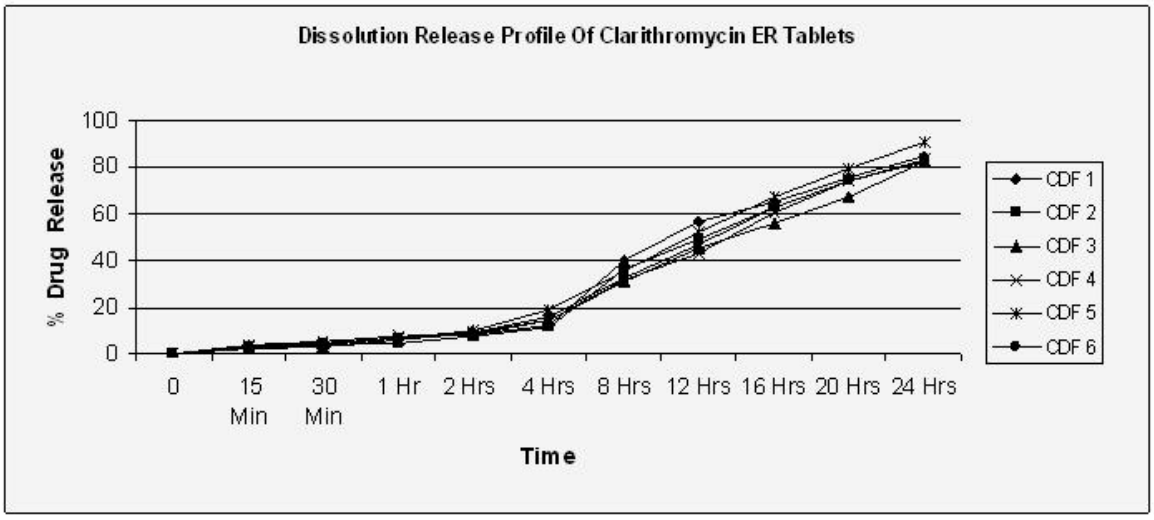

Fig. 1: Dissolution profile of Clarithromycin ER tablets

Clarithromycin tablet formulation.

Conclusion

The formulation and evaluation of extended release tablets were prepared by the trial and error method. The prepared tablets shown satisfactory results for various physicochemical evaluation tests like tablet dimensions, hardness, and weight variation. Content uniformity and In-vitro dissolution study. Tablets contain polymers such as MCC, HPMC 6CPS, PEG 6000 has shown better bioavailability and control over drug release for over the periods of 24Hrs.

Reference

[1] Shah S., Qaqish R., Patel V., Amiji M., J. Pharm. Pharmacol., 51, 667—672 (1999).

[2] Rajinikanth P. S., Balasubramanium J., Mishra B., *Int. J. Pharm.*, **335**, 114—122 (2007).

[3] Rajinikanth P. S., Mishra B., *Drug Dev. Ind. Pharm.*, **34**, 577—587, (2008).

[4] Rajinikanth P. S., Mishra B., *J. Controlled Release*, **125**, 33—41, (2008).
[5] Katayama H., Nishimura T., Ochi S., Tsuruta Y., Yamazaki Y., Shibata,K., Yoshitomi H., *Biol. Pharm. Bull.*, **22**, 55—60 (1999).
[6] Whitehead L., Fell J. T., Collett J. H., Sharma H. L., Smith A. M., *J. Controlled Release*, **55**, 3—12 (1998).
[7] Rajinikanth P. S., Mishra B., *Acta Pharm.*, **57**, 413—427 (2007).