AJMBR

AlQalam Journal of Medical and Biological Research

1

AlQalam Journal of Medical and Biological Research,2017;1(1):25-30
LN: 207/2015

Available Online: http://www.utripoli.edu.ly

Sustained Release of Amoxicilline Trihydrate for Oral Drug Delivery System

Abdulrhman. A. Akasha,
Department of Pharmaceutics, Faculty of Pharmacy, Tripoli University, Libya, P. O Box 13645.
Email: *Akashaabdu@yahoo.co.uk*

Received:11,07,2017 ***Accepted: 21,07,2017***

ABSTRACT

Background**:** *Biodegradable macroparticles may develop improved drug delivery system to gastrointestinal tract, for treatment of Helicobacter pylori, included peptic ulcers. Amoxicillin trihydrate macrocapsules have the ability to produce this effect for extended period, were prepared with bees wax as matrix using solvent evaporation techniques, to produce there different 25%, 50% and 75% coating macrocapsules. Macroparticles were examined by optical microscopy and showed spherical shape, The size of particles was determined by using sieve technique and the average size found 350 mm for all batches. IR study was carried out to check the compatibility between the selected polymer (Bees wax) and Amoxicillin Trihydrate. This study was performed to assure that there is complete physical entrapment of the drug into the polymer without any mutual interaction.* ***Methods***: *Initial in vitro experiments were under taken to examine the degradation rate in phosphate buffer at 37 ºC & PH 5.2 the process was followed up to 8 hours by which 34%, 75% and 25% of particles mass had eroded for 25%, 50% and 75% coating macrocapsules respectively.* ***Results*****:** *However the release of amoxicillin trihydrate occurred gradually sustained release 88%, 47% and 50% up to eight hours for 25%, 50% and 75% coating batches, respectively compared to the control of amoxicillin which completely released from the first hour.* ***Conclusion*****:** *The macroparticles and control were subjected to microbiological test, the Amoxicillin trihydrate and the three formulation were effective against non-pathogenic bacterial strains of Staphylococcus aureus and E.coli but not effective to more resistance bacteria such as P. aeruginosa.*

Keywords: ***Amoxicillin, Macrocapsules, bees wax, Staphylococcus aureus, E.coli and P. aeruginosa.***

INTRODUCTION

Amoxicillin Trihydrate (α-amino-hydroxybenzylpenicillin) is a semi synthetic, antibiotic [1]. Amoxicillin is in a class of medications called penicillin-like antibiotics. It works by stopping the growth of bacteria. It is a moderate spectrum, bacteriolytic, β-lactum antibiotics used to treat bacterial infections caused by susceptible microorganisms. It is effective for bacterial infection, especially for *Helicobacter pylori* infection. *Helicobacter pylori* is a major causative agent of diseases such as tonsillitis, pneumonia, bronchitis, gonorrhea, ear infections, genital, urethral infections in male/ females, stomach or duodenal ulcer and skin infection [2]. It is usually the drug of choice within the class because it is better absorbed, following oral administration, than other β-lactam antibiotics. This drug acts by inhibiting the synthesis of bacterial cell walls.

Helicobacter pylori are bacterium can infect the lining of the stomach and duodenum. Spiral-shaped, gram negative bacterium *H. pylori* found in colonized gastric mucosa or adherent to the epithelial linings of the stomach [2]. Many antimicrobial agents, such as penicillin and erythromycin, degrade rapidly in an acidic environment. It is therefore necessary to design drug delivery systems that cannot only alleviate the shortcomings of conventional delivery vehicles but also deliver the antimicrobials to the infected cell lines. 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 (from blood).

A preparation that spreads out, adheres to the gastric

Cite this article: Abdulrhman. A. Akasha. Sustained release of amoxicilline trihydrate for oral drug delivery system. Alq J Med Bio Res, 2017;1(1):25-30.

mucosal surface, and continuously releases antibiotic should be highly effective against *H. pylori*. Various mucoadhesive drug delivery systems have been proposed in *H. pylori* eradication, such as carboxyvinyl mucoadhesive microspheres [3], chitosan microspheres [4], Eudragit floating microspheres [5] and cholestyramine microcapsules [6].

Macrocasule carrier systems made from the naturally occurring biodegradable polymers have attracted considerable attention for several years in sustained drug delivery (Figure: 1). Recently, dosage forms that can precisely control the release rates and target drugs to a specific body site have made an enormous impact in the formulation and development of novel drug delivery systems. Macrocapsules form an important part of such novel drug delivery systems [7, 8]. They have varied applications and are prepared using assorted polymers [9]. In context of the above principles, a strong need was felt to develop a dosage form that delivered amoxicillin in the stomach and would increase the efficiency of the drug, providing sustained action. Thus, an attempt was made in the present investigation to use Bess wax as polymer and prepare amoxicillin macrocapsules in variable polymer coating percentages. The macrocapsules were characterized by in vitro and factorial design was used to optimize the variables.

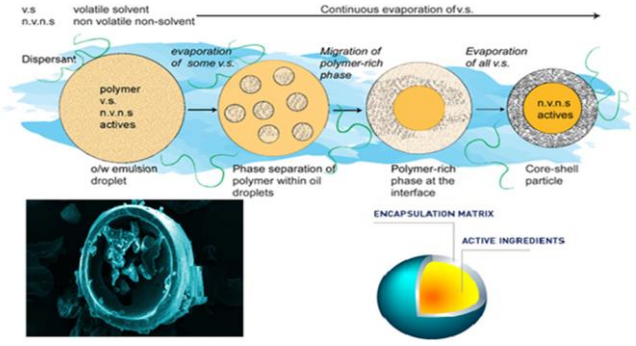

Figure 1: Diagram explains the sustained release of drug from macrocasules

METHODOLOGY

Materials

Amoxicillin trihydrate (powder) was obtained as gift sample from Asia co., Aman. Bees wax was procured from BDH, England. Chloroform was procured from Riedel-De Haen AG, Germany.

Methods

Preparation of Macrospherical matrix of Amoxicillin Trihydrate

To prepare 25% coating, of bees wax was dissolved in 15 ml of chloroform by gently heating on water bath (GFL, Germany), then of amoxicillin were dispersed in the bees wax solution. The amoxicillin suspension was added drop wise at rate of 30 drops/min, using a pipette (1 mm orifice), to 300 ml of saturated aqueous solution of amoxicillin(to prevent any further dissolution of amoxicillin at a continuous stirring rate of 5000 rpm by Ultra-turrax (IKA®- WERKE, Germany).

The system was agitated continuously for 2 hours by using magnetic stirrer (laboratwchnik, USA), to evaporate chloroform and to harden the agglomerates. The experiment was repeated using of bees wax and amoxicillin to prepare 50%, 75% coating respectively. The resultant agglomerates were filtered and dried for 24 hrs at 40ºC. The average diameter of the dried agglomerates was determined by sieving method using a range of standard sieves of 355-2000 um mesh for 10 min.

Amoxicillin drug content in macrocapsules

To determine the amoxicillin contents of the prepared microcapsules, three portions, 50 mg each of the prepared microcapsules were dissolved in 50 ml distilled water by gently heating on water bath at 90ºC. The solutions were then rapidly cooled to room temperature and 1 ml samples of solution were assayed for the amoxicillin content and compared to standard aqueous solution of amoxicillin of (1mg /ml). The results are shown in Table 2.

In-vitro drug release and polymer degradation

Appropriate amounts of microspheres (100mg) containing incorporated drug (amoxicillin base) were placed in series of tubes containing phosphate buffer pH 5.2. The samples were incubated at 37°c and gently agitated on an end-over shaker at 22 rpm. Samples were taken periodically (until all of the incorporated drug was released) and centrifuged at 3500 rpm. The supernatant was analyzed at wavelengths 325nm for amoxicillin base using a UV-spectrophotometer (JENWAY, U.K), Table 3.

The degradation rates were also measured by determining microspheres weight loss during the same experiment. After the samples were centrifuged, the

microspheres were dried and re-weighed to calculate the weight loss. The result are showed in Table 4.

Particle size analysis by sieving method

To perform particle size and particle size distribution is carried out by sieve test analysis. The dry sieves are weighed and stacked with the largest apertures at the top and the smallest at the bottom. A sample of macrocapsulated powder is placed on the top sieve and shaken for 10 minutes. The particle diameter is calculated by the following equation:

Diameter of particles = upper sieve + lower sieve / 2

% W/W = weight of particles in each fraction x 100 / Total weight of sample

Mean of particle diameter = $\sum d2X / \sum x$

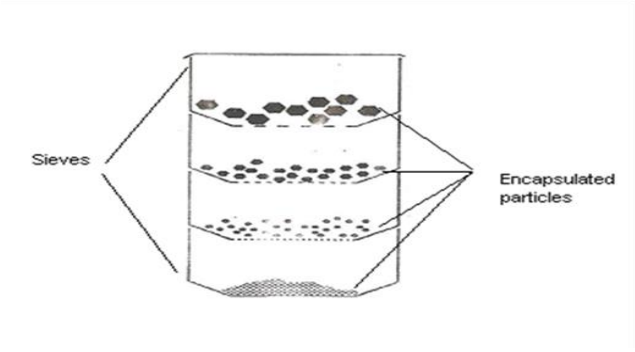

Figure 2: Sieving method analysis of macrocapules prepared by solvent evaporation method.

Infrared Spectrophotometry

IR Spectroscopy is used for recording spectra in the region of 4000-650 cm-1 (2.5-15.4 µm) or in some cases down to 200 cm-1 (50 µm).

Triturate 1-2 mg of the substance to be examined with 300-400 mg of finely powdered and dried potassium bromide R. These quantities are usually sufficient to give a disc of 10-15 mm diameter and a spectrum of suitable intensity . Carefully grind the mixture, spread it uniformly in a suitable die, and submit it to a pressure of about 800 MPa (8 t•cm-2).

Microbiological test

The antibacterial activity of the macrocapsule containing amoxicillin trihydrate was determined by using the agar well diffusion technique. Mueller Hinton agar plates were seeded with 0.1ml bacterial suspension(107-108 CFU/ml). The seeded plate were incubated 18 hrs at 37°C. The plate wells were made by sterile standard cork-borer. Each well filled with 100 mg of deferent macrocapsule formulations containing amoxicillin (25%,50% and 75% coating martial). Then bacterial plates were incubated at 37°C for 24 hrs, and the diameter of inhibition zones measured.

RESULTS

Characterization of Amoxicillin macrocapsules

Table 1: Characterization of Amoxicillin microcapsule containing amoxicillin trihydrate

Batch	Mean size	Microcapsules examination	Color	Yield
25% 50% 75%	350mm	Spherical	Off white	42.25% 81.3% 80.5%

In-vitro release of Amoxicillin trihydrate from Macrocapsules and polymer degradation.

Table 2: Drug content of amoxicillin trihydrate of all formulation

	Formulation I (25%)	Formulation II (50%)	Formulation III (75%)
Absorbance	0.9	1.8	0.4
Concentration (µg/ml)	36	72	16

Table 3. In -vitro release profiles (cumulative% Drug release) of formulations

Pure Amoxacilline		Formulation I (25 %)		Formulation II (50 %)		Formulation III (75 %)	
Conc. µg/ml	% released	Conc. µg/ml	%released	Conc. µg/ml	% released	Conc. µg/ml	% released
4.8	100	7.2	20	4.8	6.6	4.0	25
_	_	28	77	28	38	4.0	25
_	_	32	88	34	47	5.4	33.7
_	_	32	88	34	47	8.0	50

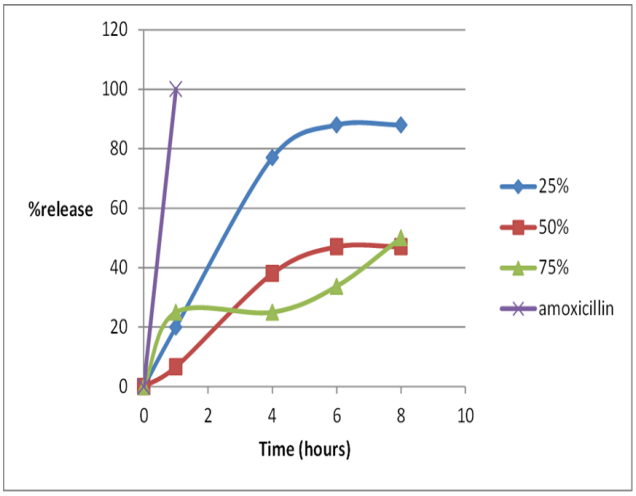

Figure 3: In -vitro release profiles (cumulative % Drug release) of formulations.

Table 4. Degradation rate of macrocapsules formulation containing amoxicillin trihydrate

	Formulation I (25 %)		Formulation I (25 %)		Formulation I (25 %)	
Time (hrs)	weight (mg)	% weight loss (mg)	weight (mg)	% weight loss (mg)	weight (mg)	% weight loss (mg)
1	89	11	50	50	89	11
4	84	16	49	51	85	15
6	81	19	30	70	84	16
8	66	34	25	75	75	25

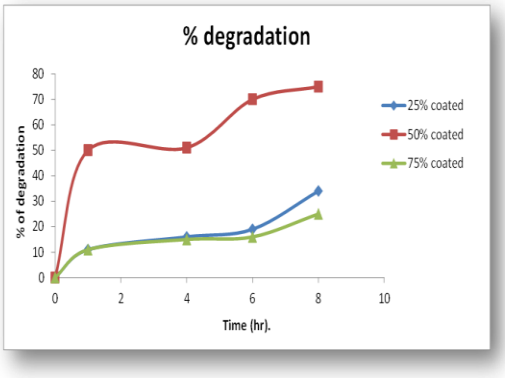

Figure 4. Degradation rate of macrocapsules formulation containing amoxicillin trihydrate

Infra Red Study

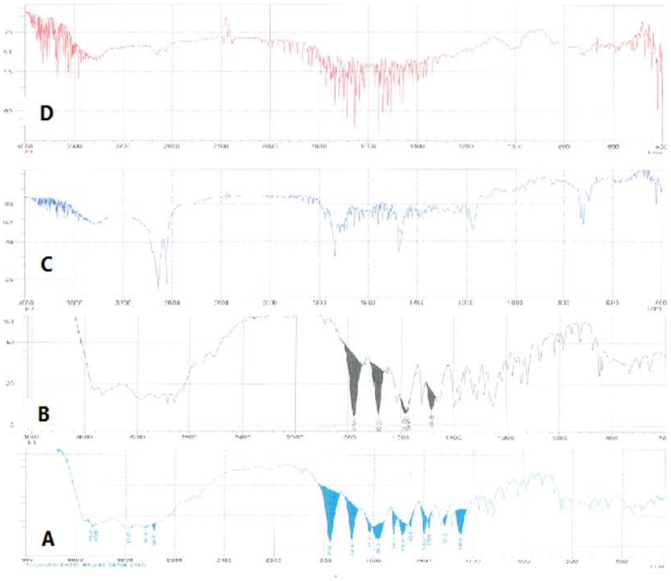

Figure 5. Overlay of IR spectra, (a) Control amoxicillin trihydrate, (b) F1 (25 %), (c) F2 (50 %), (d) F3 (75 %)

Microbiological study

Table 5. Comparative activity Amoxicillin Trihydrate and Its three formulations (25%, 50% & 75% coatings) against non-pathogenic bacterial strains

	Staphylococcus aureus Inhibition zone	*E. coli* Inhibition zone	*P.areugenosa* Inhibition zone
Blank (Phenol)	+ve (3.8)	+ve (1.5)	+ve (2.3)
Control Pure Amoxicillin	+ve (3.6)	+ve (2.0)	-ve
Formulation I	+ve (3.8)	+ve (1.2)	-ve
Formulation II	+ve (3.5)	+ve (1.0)	-ve
Formulation III	+ve (2.7)	+ve (1.0)	-ve

DISCUSSION

Macroparticles carrier systems made from naturally occurring biodegradable polymer have attracted attention for several sustained drug delivery.

Macrocapsules were (25%, 50% & 75%coating), prepared by solvent evaporation techniques, sized and the average size was calculated.

The average size was found 350 mm for all batches as shown in Table 1. The microscopically observation reveal the drug coated with bees wax in macrocapsules in general appear reasonably in their appearances. The drug entrapment efficiency analysis showed that the entrapment of drug within each batch of microspheres Table2. The percentage yield of microspheres of all formulation was in the range from 42.25% to 81.5%. The Macrocapsules prepared by this method was found to be discreet, spherical, and it was observed by optical microscopy Table 1.

The drug content determination shows that even if the polymer composition was changed (25%, 50% & 75% coating), the process was highly efficient to give macrocapsules having maximum drug loading Table 1.

In-vitro drug release studies were carried out with formulations in phosphate buffer solution. At the lowest concentration of the polymer the drug release from 25% coating formulation was within eight was faster than the other concentration of the polymer increased up to maximum extent the drug release. The in-vitro release data have been plotted according to the following models of data treatment, cumulative percent drug release versus time, the drug polymer ratio has an impact on the drug encapsulation efficiency and in vitro.

The slow release of amoxicillin trihydrate may support the view that the drug is coated deeper inside the macrocapsules for all formulation as show in Table3, Figure3.

It observed that the increase in the concentration of the polymer increase the entrapment efficacy as the comparison between batch 25% coating 50% coating, 75% coating material (10). Since 88% of amoxicillin was released up to 8hrs,while at the same time 47%, 50% released for 50%, 75% respectively.

This observation suggests that, the high concentration of coating is the slow release rate of the drug as shown in Table 3, Figure 3.

The degradation rate of bees wax is followed up to 8hrs by which time up to 75%of microcapsules mass had eroded for 50% coating material. while ,the other have shown lees erosion as shown in 25% & 75% with 34 & 25 % of degradation rate Table 4 , Figure 4.

It seems that the slow degradation of amoxicillin-loaded macrocapsules has successful controlled release of drug for oral delivery.

IR study was carried out to check the compatibility between the selected polymer Bees wax and Amoxicillin Trihydrate. All the spectra were compared for shifting of major functional peaks and also for the loss of functional peaks, if any. Amide group band (3500-3118 cm-1) , Imine group band (1690-1640 cm-1), Carbonyl amide group band (1680-1630 cm-1), Carboxylic group band (1730-1700 cm-1) are shown in the spectra.

When the spectra compared with the library, it was found out that, there was no shifting of functional peaks and no overlapping of characteristic peaks and also there was no appearance of new peaks. No significant change in the IR spectra of Amoxicillin Trihydrate-macrocapsules were observed, except for the broadening of the peaks as shown in Figure 5.

Furthermore, amoxicillin trihydrate and the three formulation were subjected for the antimicrobial tests showed: All formulations and the pure amoxicillin were effective against non-pathogenic bacterial strains of Staphylococcus aureus and E.coli but not effective to more resistance bacteria such as *P. aeruginosa*, as shown in Table 5.

All formulations shown suitable size range to be administered orally for controlled release and can remain for longer time in the GIT. The Formulation 50% and 75% had release up to 8 hours and more entrapments still in the macroparticles to be carried.

CONCLUSION

The study provides evidence to support view that macrocapsules prepared by natural polymers such as bees wax produce macrocapsules for oral drug delivery .It is important to prepare several formulations with different polymer concentration to compare the release profile as well as degradation rate.

DISCLOSURE STATEMENT

Conflict of interest statement was not declared.

ACKNOWLEDGEMENT

The author would like to express our thanks to department of pharmaceutics, faculty of Pharmacy University of Tripoli and Tripoli Center of Drug & Food

quality Control and specifications, for Their help and support.

REFERENCES

1. Pandit.V, Suresh.S, Joshi.H. Gastro retentive drug delivery system of amoxicillin: formulation and in vitro evaluation, Int. J.Pharma.Chem.(2010);1:1-10.
2. Linda NM, Douglas JB. Management of Helicobacter pylori infection. American family physician. 2002; 65(7): 1327-1339
3. Nagahara N, Akiyama Y, Tada M, Nakao M, Kitano M, Ogawa Y. Mucoadhesive microspheres containing amoxycillin for clearance of Helicobacter pylori. Antimicrob Agents Chemother. 1998;42:2492-2494.
4. Hejazi R, Amiji M. Stomach-specific anti-*H. pylori* therapy, I: preparation and characterization of tetracycline-loaded chitosan microspheres. Int J Pharm. 2002;235:87-94.
5. Umamaheshwari RB, Jain S, Jain NK. A new approach in gastroretentive drug delivery system using cholestyramine. Drug Deliv. 2003;10:151-160.
6. Umamaheshwari RB, Jain S, Tripathi PK, Agrawal GP, Jain NK. Floating-bioadhesive microspheres containing acetohydroxamic acid for the clearance of Helicobacter pylori. Drug Deliv. 2002;9:221-233.
7. Gohel, M.C.; Amin, A.F.; J. Control. Release, 1998, 51, 115-122.
8. Capan, Y.; Jiang, G.; Giovagnoli, S.; DeLuca, P.P. AAPS PharmSciTech., 2003, 4, article 28.
9. Vasir, J.K.; Tambwekar, K.; Garg, S. Int. J. Pharm., 2003, 255, 1332.
10. Yellankis.k,Singh J, Syed J.A,Bigala R,Gorantis and Kumarnerella N.Designand and characterization of amoxicillin trihydrate mucoadhesive microsopheres for porolonged gastric retention .Int J.pharm .SCISD .RES ,(2010);2(2):112-114.