Effect of coating method on release of Glimepiride from porosity osmotic pump tablets (POPTs)

Nuha Mohammed abdulkhaleq*, Wedad K. Ali*, Amal A. Elkordy**
Department of Pharmaceutics, College of Pharmacy, Al-Mustansiriyah University/Iraq.
***** Sunderland University, UK***

DOI: https://doi.org/10.32947/ajps.20.02.0448

Article Info:

Received 16 Mar 2020
Accepted 26 Apr 2020
Published 1 May 2020

Corresponding Author email:
pharm.dr.wedad.ali.@uomustansiriyah.edu.iq
orcid: https://orcid.org/0000-0003-2522-5428

Abstract

In this study, once-daily porosity osmotic pump tablets (POPTs) of Glimepiride were prepared using HPMC K100M (61%), osmotic agent (30% NaCl) coated using two different coating techniques spraying and dipping methods. The coating solution composed of ethyl cellulose (7.5%) w\w in ethanol (90%), castor oil (2%) as water-insoluble plasticizer and Gingo red color (0.5% w\w). In both techniques, the coating level was adjusted to give a 10% increase in the weight of the tablets. The effect of the coating by dipping technique with an increase in the weight of tablet (10 %, 20% & 50%) was also investigated to see the effect coating level on the percentage of drug release from POPTs.

The results of the in vitro release of Glimepiride from tablets coated by the spraying method showed longer release time (24 hrs) than those coated with dipping method. On the other hand, increasing the coating level by dipping method retarded the release of the drug from tablets. However, the same retardation effect on release as shown with the spraying technique was only obtained by increasing the coating level with a 50% increase in the weight of the tablet. Thus, coating by spraying is more efficient to prepare POPTs to give a continuous release of Glimepiride from once daily table with the lowest increase in the total weight of the tablet.

Key words: Glimepiride, porosity osmotic pump tablets, a dipping method, spray drying

تاثير طريقة التغليف على تحرر غليمبيريد من الحبوب المضخة الازموزية المسامية

نهى محمد عبد الخالق* ,وداد كمال علي *, أمال علي الكوردي**
***الجامعة المستنصرية كلية الصيدلة/ فرع الصيدلانيات**
**** جامعة ساندرلاند/ المملكة المتحدة**

الخلاصة:

في هذه الدراسة تم تحضير الحبوب المضخة الازموزية المسامية للغليمبيريد لتاخذ كجرعة واحدة باليوم باستخدام هايدروكسي بروبيل مثيل سلسلوز 61% ومادة العاملة للازموزية 30% كلوريد الصوديوم وتغليفها بطريقتين وهما الغمس والزذاذ المجفف. محلول التغليف احتوت على المثيل سلسلوز بنسبة7.5% في الايثانول 90% و زيت الخرع كمادة ملدنة بنسبة 2% و كيغو الاحمر بنسبة 0.5% كمادة ملونة. في كلتا الطريقتين تم السيطرة على ان تكون نسبة الزيادة في وزن الحبة 10% باستخدام التغليف. كما تم استقصاء تاثير الزيادات المختلفة في وزن الحبة باستخدام طريقة الغمس (10%, 20% و50%) على تحرر الدواء من الحبوب الضعط الازموزية التناضحية.

اضهرت نتائج تحرر الدواء خارج الجسم بان الحبوب التي تم تغليفها بالرذاذ النجفف قد اعطت فترة تحرر اطول (24 ساعة) مقارنة مع التي تم تغليفها بالغمس. من ناحية اخرى زيادة مستوى التغليف بطريقة الغمس ادت الى بطئ في تحرر الدواء من الحبوب. الا انه لم يتم الحصول على نفس تباطئ بتحرر الدواء مثل التي لوحظ من الحبوب المغلفة بالرذاذ

المجفف الا بعد الوصول الى 50% زيادة في وزن الحبة. وعليه فان طريقة التغليف بالرذاذ تكون طريقة كفوئة للحصول على تحرر مستمر من الحبوب التي تاخذ مرة باليوم وبزيادة اقل في وزن الحبة.
الكلمات المفتاحية: غليمبيريد, الحبوب المضخة الازموزية المسامية, طريقة الغمس, الرذاذ المجفف

Introduction

The coating is an essential step in the formulation of porosity osmotic pump tablets to create osmotic pressure inside the tablets. Generally, there are two major methods for applying coat; these include pan spray drying and dipping methods. The pan coating is also known as the regular pan system which is a common accessory in almost all pharmaceutical industries for coating use. Spraying and drying equipment is usually connected to the pan coating to complete the whole coating system [1, 2].

For coating by spray drier, there are two parameters: First one related to the spraying equipment such as the number of nozzles, nozzle type & nozzle-to-nozzle distance and second, the process parameters which is included nozzle-to-bed distance, angle spray rate, atomizing and pattern air pressure [3, 4].

In coating by spray drying the coating, liquid has arrived at the tablet surfaces and the coat should dry almost instantly. To ensure a rapid drying, the supply air is directed over the pan perforations into the tablet bed. The significant parameters contain the supply air humidity & temperature, pan perforations & supply air volume. Excessive moisture can be prevented through the appropriate settings [4, 5].

Drying performance can be influenced and optimized by the type of airflow during coating. Draining air & directing supply air over the tablet bed decreases turbulence & creates a cold environment area. A high sensitivity degree of drying cycles to changes in environmental humidity was demonstrated by the apparatus. It is consequently, felt a moisture-sensing device ought to be utilized when considering an automatic tablet-coating system for tablets production [4, 6].

The advantages of pan spray drier are quality control, speed, and increase tablets acceptability & elegancy. While, one disadvantage of pan spray drier is its high cost [4, 7].

For more than forty years Schott developed a dipping technique to create dielectric thin films on tablet core by immersion the tablet cores into the coat solution several times then drying by hot air until getting the wanted weight [8]. This coating is applied by dipping the tablets into coating liquid and then the wet tablets are dried by hot air. Alternate dipping and drying steps may be repeated numerous times to achieve coating properties [9].

The porosity osmotic pump tablets (POPTs) is one type of sustained-release tablets mostly used to administer drug intended to treat chronic diseases such as diabetic, hypertension, asthma and others disease to increases patient compliance by reducing the number of administrated doses and minimizing the chance to miss any dose taken during the day by the patient [10].

In this study, porosity osmotic pump tablets were formulated to provide a single dose of Glimepiride (8mg) as sustain release dosage form to increase patient compliance with diabetes mellitus type II [11]. While the aim of this study to investigate the effect of coating method dipping and spray drier on drug release from porosity osmotic pump tablets.

Material and methods

Materials:

Glimepiride (Shanghai, China) was chosen as an active pharmaceutical ingredient for porosity osmotic pump tablets; Ethylcellulose polymer used in coat preparations (Shanghai, China). Castor oil (Samara drug industry, Iraq) was selected as plasticizer while Gingo red color was obtained from (Leverkusen, Germany) and the solvent used in coat preparation was ethanol (Hayman group, UK). The materials of tablet cores were HPMC

K100M (Shin-Etsu Chemicals Co.Ltd., Japan), Sodium chloride was the osmotic agent from (Samara drug industry, Iraq), Talc as glidant agent (Samara drug industry, Iraq) and Mg. stearate used as a lubricant from (Samara drug industry, Iraq).

Method

Preparation of powder blends for core tablets:

Tablet cores containing Glimepiride (8mg/tablet) were prepared with other compositions listed in Table (1). Sodium chloride was pre-screened via a sieve with a 120µ pores size. Magnesium stearate and talc were similarly screened via a sieve with 250µ pores size. All the components were mixed for 15 min and sieved via a mesh with a 420µ pores size with five times repeating the sieving.

Table (1): Formulas of Glimepiride core into Porosity Osmotic Pump Tablet:

Ingredient	Concentration (mg)
Glimepiride	8
Talc	0.5
Mg. stearate	0.5
NaCl	30
HPMC K100M	61

Preparation of Glimepiride in porosity osmotic pump tablets

Preparation of core tablets:

Tablets were directly compressed from the mixture using 6.1 mm concaved punches and die in a tablet machine.

Preparation of coated solution [12, 13]

The coated polymer solution was prepared by soaking and stirring ethylcellulose in ethanol (90%) on a magnetic stirrer for 12 h to obtain a 7.5% w\w coating solution. Castor oil (2%) was then added further the solution stirred for 2h. finally, Gingo red color (0.5% w\w) was added with stirring continued for 2h.

Coated the cores tablets:

A-spray drying technique [12, 13]

Firstly, the prepared tablet cores were placed in the pan for 15 min to warming the tablet cores using hot air before applying the spraying coat solution onto the tablet surfaces by spray drying technique. The flow of hot air was used to aid in fixing the coating material droplet on the tablet cores, the parameters for spray drier summarized in Table (2). After the complete procedure of spraying and drying all coated tablets were transferred to an oven of 40 °C for 4hr to ensure the removal of ethanol by evaporation.

Finally, the total weight of tablets in this method was 110 mg only a 10% increase in tablets weight and this percent provides the wanted time (24 hrs) for drug release that leads to only this percent of weight gained.

Table (2): Spray drier parameters:

Condition	Parameter
The diameter of the nozzle orifice	0.1 mm
Spray rate	2ml/min
Product temperature	40-44 °C
Rotating rate of pan	20 rpm
Spray air pressure	4Kg /cm^2
Stirring speed	50 rpm

B- Dipping technique [14]

To prepare coated tablets by dipping method, tablets were immersed in coating solution by dipping several times and drying them after each immersion with hot air until getting the wanted gained weight (10 %, 20% & 50%) so the total weight respectively (110 mg, 120 mg & 150 mg).

Diameter and thickness of coat [15]:

The thickness and diameter of the core and coated tablets by spraying and dipping methods were determined for 10 tablets which were selected using a diameter vernier caliper. The cross-sectional image of coated tablets was captured by a digital microscope to see the difference between the two methods of coatings.

Hardness [16]:

Three tablets from each POP tablets were selected randomly and their hardness was tested by hardness tester (china) by placing them between moving and fixed jaw.

The scale of hardness tester was adjusted to zero and slowly increase the total force until the tablets fractured, the force point was recorded to represent the hardness expressed by Kg/cm^2.

In-vitro Dissolution Test [17]

The dissolution test was done to determine the rate of release of Glimepiride from Porosity Osmotic Pump tablets using the USP basket method (Dissolution apparatus I) [18]. Dissolution study continued for 24 hrs, the formulated tablets were placed first in 0.1 N HCl for 2 hrs then were transferred to phosphate buffer (pH 6.8) for 4 hrs and for 18 hrs in phosphate buffer (PH 7.4) to complete 24 hrs. The basket was rotated at 50 rpm and the temperature of the dissolution medium was maintained at 37±0.5°C. At the following time intervals 5, 10, 15, 30 then every 30 (min), 5ml from dissolution medium was withdrawn and replaced by the same volume with fresh dissolution medium. The withdrawn samples were then filtered using filter paper (Toppan Shoji Go., LTD) and diluted by either 0.1 N HCl or phosphate buffer (pH 6.8 & 7.4), to measure the absorbance by UV-Vis spectrophotometer (China) at λmax (225 nm) of the drug. The concentration of the drug in each withdrawn sample was determined using the calibration curves of the drug in dissolution media used in this test.

Results and Discussions

Diameter and thickness of POPTs:

The diameter of core tablets depends on the diameter of punches and die that used in a tablet machine, while the diameter of coated tablets depends on the method of coat that applied on tablet cores which include dipping and spray drying methods that were used in this research because each had different parameters.

The diameter of the formulation coated by the spray drier method with 10 % weight gained (FS10) was 6.5 ± 0.01 (mm), while the diameter of 10 % weight gained by a dipping method (FD10) was 6.4 ± 0.1. It is clear that there was no difference in diameter of tablets obtained by the either spraying or dipping method with the same weight gained because the weight gained when increase leads to the diameter of tablets as shown in Table (3) when increasing weight gained as in formulation coated by dipping method with 20% and 50% weight gained (FD20 & FD50) lead to increase the diameter of tablets. Also, the cross-sectional images of coated tablets by dipping and spraying methods using digital microscope are shown in Figure (1).

Table (3): Results of a comparison study between dipping and spray drying coating techniques on the properties of POPTs.

Formulation code	Diameter of core (mm)	Method of coat application	Percentage of weight gained	Weight Gained (mg)	Diameter (mm)
FS10	6.1	Spray drying	10 %	110 ± 0.5	6.5 ± 0.01
FD10	6.1	Dipping	10 %	110 ± 0.5	6.4 ± 0.1
FD20	6.1	Dipping	20 %	120 ± 0.8	6.6 ± 0.1
FD50	6.1	Dipping	50 %	150 ± 1	7.5 ± 0.2

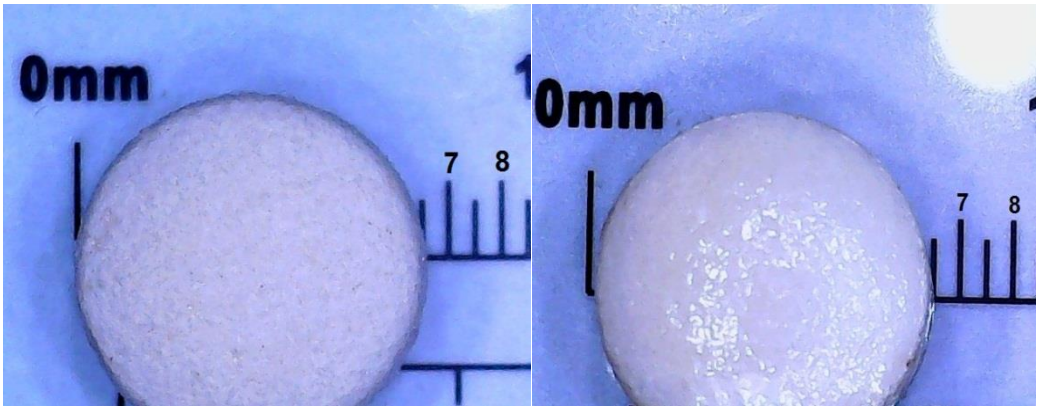

Image 1: Spray drying 10% **Image 2: Dipping 10%**

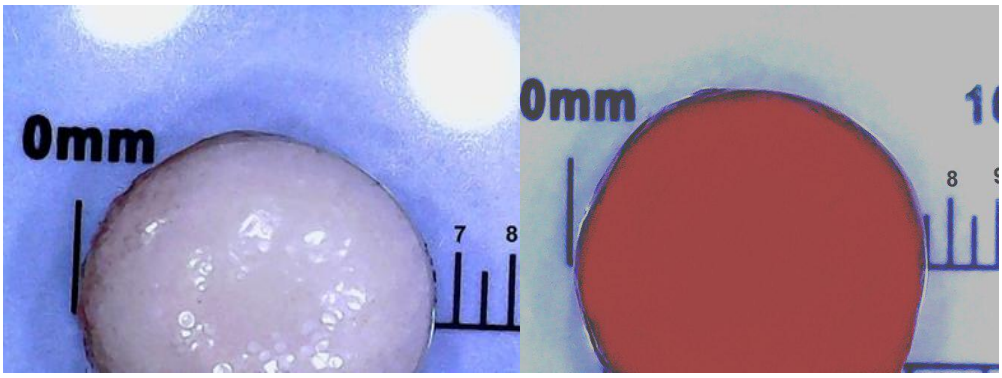

Image 3: Dipping 20% **Image 4: Dipping 50 %**

Figure (1): Images of the surface appearance of POPTs coated with different methods of coating and weight gain.

Hardness

Tablets require a certain amount of strength or hardness to beer the mechanical shocks of damage during storage, handling, transporting and shipping [19] The hardness measured by electrical hardness tester for all prepared tablets was (9.0 ± 0.5) for uncoated tablets and coated tablets. These results as certain that the tablets had sufficient strength to resistant during storage, handling, transporting, shipping and mechanical stress. Sufficient tablet

hardness and resistance to crushing and friability are important basics for the customer.

The coated tablets had the same hardness of core tablets that means the method of the coat did not affect the tablet's hardness.

In vitro evaluation of Glimepiride release from Porosity Osmotic Pump tablets

In this study, the impact of the coating method on the release from the osmotic tablets coated by spray drying technique (with 10% increase in weight of tablet) and dipping method with (10%, 20% & 50%) increased in tablets weight. The release from coated tablets with different methods with the same increase in the percentage of weight (10%) was investigated. The result showed that the release time of Glimepiride from formulated osmotic tablet and with spray drier coating was 24 hr to complete drug release, while the release time of Glimepiride from formulation coated with dipping method was 5 hr as shown in figure (2). According to the similarity factor, there was a significant difference (f<50%) between the percentage of drug released from these POPTs coated by dipping & spray drier at pH2 and phosphate buffer (pH 6.8 & 7.4). This belongs to the more homogenous coat applied by the spray drier method as shown in image 1 at the figure (1) than that coat applied by the dipping method. Spray drying coating is considered as micro coating technique since the coat introduced via the nozzle which has a diameter in micrometer scale (0.1 mm), in addition to air pressure 4 Kg\cm2 which was used to minimize the coat at the micro-scale to enter through this micropore. Upon application of coat on the core tablets homogenous multilayers in micro-scale were formed to get 10 % increased by weight [20]. The dipping includes only immersion the cores in the ordinary coat with drying occur to get a ride from the solvent [21].

The second part of the in vitro release study was investigating the impact of different weight gained by a dipping method (10%, 20% & 50 %) on drug release from POPTs. The release of drug from POPTs was delayed as the level of weight gained increased (Figure 3). This retardation in the release of the drug was related to more thickness barrier layer formation and reduced in the hydration rate of core [22]. According to the similarity factor, there were significant differences (f2<50%) between the percentages of drugs released from the dipping method. The release from tablet showed (10%) increased weight lasted for 5 hr, where release duration in case of (20%) and (50%) increased weight were 9 and 24 hr respectively. The result of the release of the drug from POPT coated by dipping (50% increase in weight) was similar to the time of the release from POPT coated by spray drier technique (weight increased by 10%) this belongs to the nature of coat that formed by spray drier more strong and more homogenous than a coat that formed by dipping method because the multilayers in micro-scale that formed in spray drier method [20].

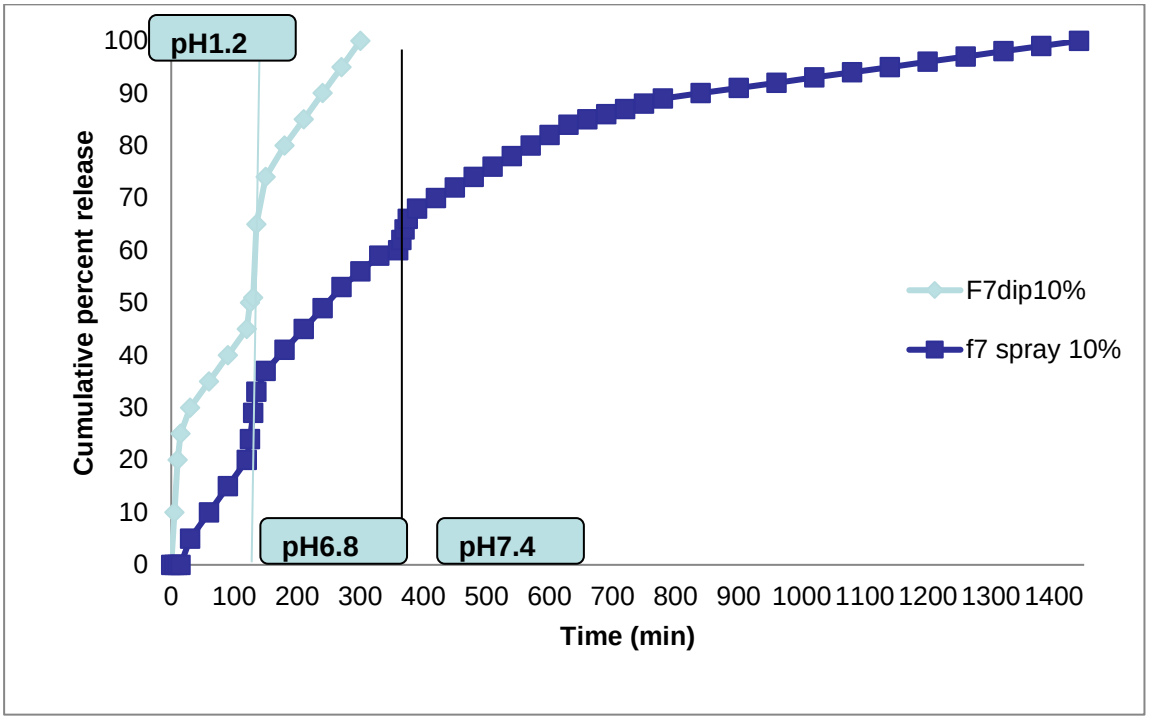

Figure (2): The effect of the coating method on in- vitro drug release from POPTs in dissolution media pH (1.2, 6.8 & 7.4) at 37°C and 50 rpm.

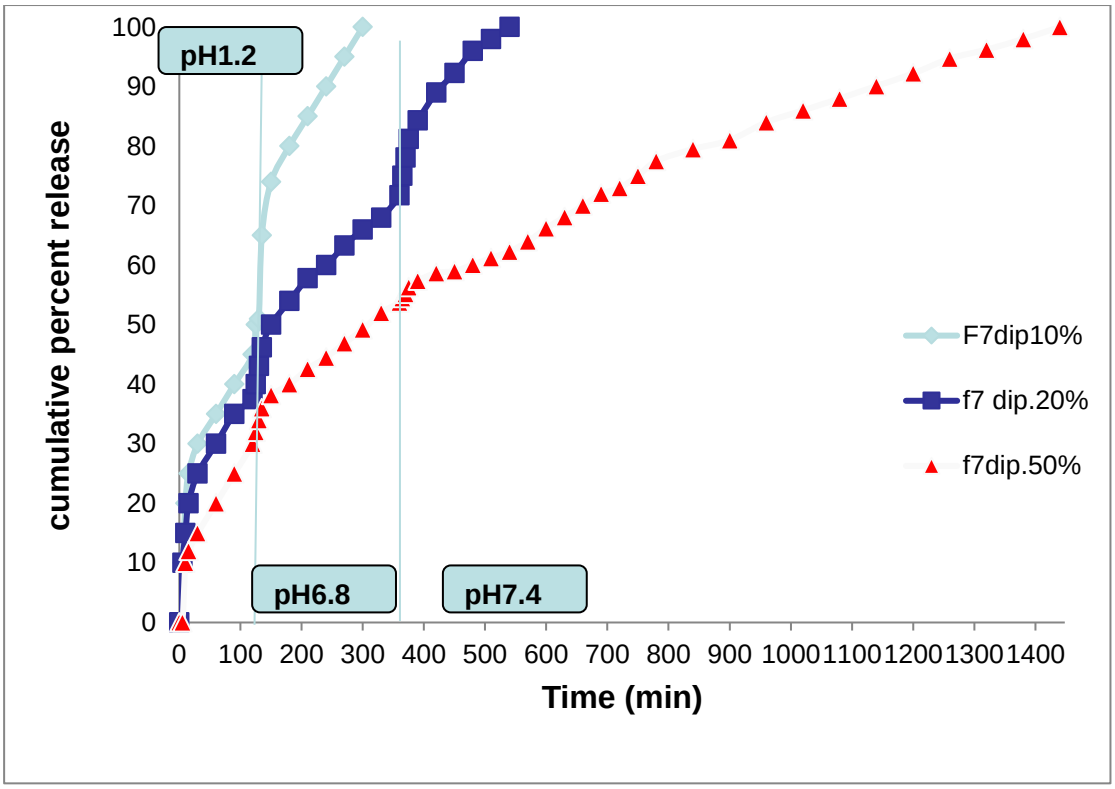

Figure (3): The effect of weight gained by dipping on in vitro drug release from POPTs in dissolution media pH (1.2, 6.8 & 7.4) at 37°C and 50 rpm.

Conclusion

The best method of coating for continuous release of Glimepiride form POPTS was spray drying method since it released the drug through 24 hr, smoother and evenly coat could be obtained with less gain in the weight of POPT than with dipping method

References

1- Babu A, RATNA PRV. Controlled-porosity osmotic pump tablets-an overview. Asian Journal of Pharmaceutical Research and Health Care. 2010;2(1)522-601.
2- Longxiao Liu, Xiangning Xu. Preparation of bilayer-core osmotic pump tablet by coating the indented core tablet. Int. J. Pham. 2008; 352, (1-2):225-230.
3- Lantz Jr RJ, Bailey A, Robinson MJ. Monitoring volatile coating solution applications in a coating pan. Journal of pharmaceutical sciences. 1970;59(8):1174-7.
4- Masters K. Current market-driven spray drying development activities. Drying technology. 2004;22(6):1351-70.
5- Patel YL, Sher P, Pawar AP. The effect of drug concentration and curing time on processing and properties of calcium alginate beads containing metronidazole by response surface methodology. AAPS PharmSciTech. 2006;7(4): E24-E30.
6- Troshko AA, Zdravistch F. CFD modeling of slurry bubble column reactors for Fisher–Tropsch synthesis. Chemical engineering science. 2009;64(5):892-903.
7- Zentner GM, Rork GS, Himmelstein KJ. The controlled porosity osmotic pump. Journal of controlled release. 1985;1(4):269-82.
8- Vitt B, Blankenburg J, Behr WJ, Dasecke K-H, Lintner B. UV-reflective interference layer system. Google. Patents; 2004.
9- Lachman leon et al. The Theory and Practice of Industrial Pharmacy. Second edition, Fourth Indian Reprint, Published by Varghese Publishing house, Bombay. 1991: 346-372.
10- Lipp R. Major advances in oral drug delivery over the past 15 years. Am Pharm Rev. 2013: 16:28-35.
11- Buckley, Nick. Australain medicines handbook. 19th. 2018.
12- Liu L, Wang X. Solubility-modulated monolithic osmotic pump tablet for atenolol delivery. European journal Macintyre of pharmaceutics and biopharmaceutics. 2008: 68(2):298-302.
13- Liu L, Xu X. Preparation of bilayer-core osmotic pump tablet by coating the indented core tablet. International journal of pharmaceutics. 2008; 352(1-2):225-30.
14- Girotra P, Singh SK. Formulation optimization for colon targeted delivery of katira gum matrix tablets containing azathioprine. International Journal of Pharmaceutical Sciences and Drug Research. 2013: 5(4):133-40.
15- Cheng L, Li T, Dong L, et al. Design and evaluation of bilayer pump tablet of flurbiprofen solid dispersion for zero-order controlled delivery. J Pharm Sci. 2018;107: 1434–1442.
16- Getyala A, V Gangadharappa H, Sarat Chandra Prasad M, Praveen Kumar Reddy M, M Pramod Kumar T. Formulation and evaluation of non-effervescent

floating tablets of losartan potassium. Current drug delivery. 2013;10(5):620-9.
17- Arti Banerjee, P. R. P. Verma. Controlled porosity solubility Modulated osmotic pump tablets of Gliclazide. Int J Pharm Sci. 2013: 2:231-42.
18- United states pharmacopea, electronic copy, 2007.
19- Ansel HC, Popovich NG, Allen LV. Pharmaceutical dosage forms and drug delivery systems: Williams & Wilkins Baltimore; 1995.
20- Wisniewski R. Spray drying technology for brine processing; System design and operation; Technology and systems review. Internal Report, NASA Ames Research Center, Moffett Field, 2014.
21- Yang, Y.; Shen, L.; Yuan, F.; Fu, H.; Shan, W. Preparation of sustained release capsules by electrostatic dry powder coating, using traditional dip coating as reference. Int. J. Pharm. 2018, 543, 345–351.
22- Spencer, J.A., Gao, Z., Morre, T., Buhse, L.F., Taday, P.F., Newnham, D.A., Shen, Y., Portieri, A., Husain, A., 2008. Delayed release tablet dissolution related to coating thickness by terahertz pulsed image mapping. J. Pharm. Sci. 97, 1543–1550.