Available online at *www.ujpronline.com*
Universal Journal of Pharmaceutical Research
An International Peer Reviewed Journal
ISSN: 2831-5235 (Print); 2456-8058 (Electronic)

RESEARCH ARTICLE

DEVELOPMENT AND EVALUATION OF ALBENDAZOLE MICROCAPSULE FOR COLONIC DRUG DELIVERY SYSTEM

Onyeka Ifeanyi Peter, Ukwe Chioma Ifeoma
Department of Pharmacognosy and Traditional Medicine, Nnamdi Azikiwe University Awka, Nigeria

Article Info:

Article History:
Received: 11 February 2017
Reviewed: 9 March 2017
Accepted: 23 April 2017
Published: 15 May 2017

Cite this article:
Peter OI, Ifeoma UC. Development and evaluation of Albendazole microcapsule for colonic drug delivery system. Universal Journal of Pharmaceutical Research 2017; 2(2): 4-7.
http://doi.org/10.22270/ujpr.v2i2.R2

***Address for Correspondence:**
Onyeka Ifeanyi Peter, Department of Pharmacognosy and Traditional Medicine, Nnamdi Azikiwe University Awka, Nigeria;
E-mail: *anyinoble2get@gmail.com*

Abstract

Objective: Albendazole is a benzimidazole carbamate broad spectrum oral anthelmetic drug. It is poorly water soluble and it undergoes extensive metabolism in the intestine and liver. Objective of present study was to prepare and evaluate microcapsule of Albendazole for colonic delivery.
Methods: Six batches of Albendazole microcapsules were prepared using different concentration of polymers like Eudragit RS-100, chitosan, HPMC by solvent evaporation method. The microcapsules were then evaluated for micromeritic properties, percentage yield, incorporation efficiency, drug content. *In vitro* dissolution profile of each formulation was determined by employing USP XXIII rotating basket method.
Results: The drug content was found to be very high in all formulations, incorporation efficiency was found to be good in all formulations. Highest incorporation efficiency 96.48 % was found in batch of MC6. Maximum drug release was shown by microcapsules formulation of batch MC6 (90.18%)
Conclusion: Study concludes that Albendazole microcapsules may prove to be potential candidate for safe and effective sustained drug delivery.
Keywords: Albendazole, colon specific, eudragit, microcapsules.

INTRODUCTION

Colon targeted drug delivery is used to deliver the drugs that are degraded by the digestive enzymes in the stomach such as proteins and peptides. The colon is attracting inter est as a site where poorly absorbed drug molecule may have an improved bioavailability[1]. Colon is recognized as having a somewhat less hostile environment with less diversity and intensity of activity as compared to stomach and small intestine[2]. Furthermore, the colon has a long retention time and appears highly responsive to agents that enhance the absorption of poorly absorbed drugs. Colon is also found to be a promising site when delay in absorption is desirable from therapeutic point of view for the treatment of disease that have peak symptoms in early morning and that exhibit circadian rhythm, such as rheumatoid arthritis, nocturnal asthma and angina pectoris. Colon targeted drug delivery of drugs reduces the systemic side effects[3]. Microencapsulation is a process in which tiny particles or a coating to give small capsules with many useful properties surrounds droplets. Furthermore the administered dose of a drug is subdivided into small units that are spread over a large area of the gastrointestinal tract, which may enhance absorption by diminishing localized drug concentration[4].

Albendazole is a benzimidazole carbamate broad spectrum oral anthelmetic used to treat a variety of worm infections caused by nematodes and cestodes[5]. It falls into the BCS class II category as has high permeability and low solubility[6]. It is poorly soluble having aqueous solubility to be 0.2 mg ml^{-1} at 25°C. Because of its low aqueous solubility, it is poorly and erratically absorbed following oral administration[7]. Following oral administration, it was found to absorb 1–5%, and it undergoes extensive metabolism in the intestine and liver[8]. It is further metabolized into albendazole sulfone which is pharmacologically inactive[9]. In present study microcapsules of Albendazole were formulated for colonic drug delivery to avoid side effects associated with albendazole therapy and to improve pharmacological effect as most of the worms reside in large intestinal part and.

MATERIALS AND METHODS

Albendazole was obtained from Emzor Pharmaceutical Industries Limited, Lagos Eudragit RS-100 was

obtained from Evans Medical PLC, Lagos, Nigeria, HPMC and chitosan were obtained from Revive Technologies, lagos. All other chemicals and reagent used in this study were of analytical grade.

Method of preparation

Albendazole microcapsules formulations were prepared by solvent evaporation method[10]. Accurately weighted Eudragit RS-100, chitosan and HPMC were taken in different ratios as shown in Table 1. All polymers were dissolved in 30ml of acetone to form a homogenous polymers solution. Core material, i.e. Albendazole was dispersed in it and mixed thoroughly. This organic phase was slowly poured at 15°C in to liquid paraffin (100 ml) containing 1% (w/w) of Span-80 with stirring at 1000 rpm to form a uniform emulsion. Thereafter, it was allowed to attain room temperature and stirring was continued until residual acetone evaporated and smooth-walled, rigid and discrete microcapsules were formed. The microcapsules were collected by decantation and the product was washed with petroleum ether (40–60°C), four times and dried at room temperature for 3 hrs. The microcapsules were then stored in a desiccators over fused calcium chloride.

Table 1: Composition of Albendazole microcapsules.

Code	Drug (mg)	Eudragit RS-100 (mg)	Chitosan (mg)	HPMC (mg)	Liquid paraffin (ml)	Span 80 (ml)	Acetone (ml)
MC1	400	300	-	-	50	1	30
MC2	400	-	300	-	50	1	30
MC3	400	-	-	300	50	1	30
MC4	400	200	100	-	50	1	30
MC5	400	-	200	100	50	1	30
MC6	400	200	100	200	50	1	30

Evaluation of albendazole microcapsules

Micromeritic properties

The microcapsules are characterized by their micromeritic properties such as bulk density, true density, porosity, Hausner's ratio[11].

Particle size

Determination of average particle size of the Albendazole microcapsules was carried out by the optical microscopy method. A minute quantity of microcapsules was spread on clean glass slide and average sizes of 100 microcapsules were determined in each batch[12].

Percentage yield

The measured weight was divided by total amount of all non-volatile components which were used for the preparation of microcapsule[13].

$$\% \text{ yield} = \frac{\text{Actual weight of product}}{\text{Total weight of excipient and drug}} X\ 100$$

Incorporation efficiency:

In 100 ml volumetric flask 25mg of crushed microcapsules were taken and dissolved with small quantity of ethanol of the volume is made up to mark with pH 6.8 and stirred for 12 hours. After stirring the solution was filtered through Whatman filter paper and from the filtrate appropriate dilutions were made and absorbance was measured at 261 nm by using UV-spectrophotometer[14].

Drug content

In a 100 ml volumetric flask, 25 mg of crushed microcapsules were taken, and volume was made up to mark with pH 7.4. The flask was shaken for 12 hours using an orbital shaker incubator. Then the solution was filtered and from the filtrate appropriate dilutions were made and absorbance was measured at 261 nm[15].

***In vitro* release studies:**

In vitro dissolution profile of each formulation was determined by employing USP XXIII rotating basket method (900 ml of pH 6.8-phosphate buffer, 100 rpm, 37±0.5°C). Microcapsules equivalent to 150 mg of Albendazole was loaded into the basket of the dissolution apparatus. Five milliliters of the sample was withdrawn from the dissolution media at suitable time intervals and the same amount was replaced with fresh buffer. The absorbance of the filtrate was determined at wavelength of 261 nm by using UV spectrophotometer, against pH 6.8 as blank[16].

Statistical analysis

Experimental results were expressed as mean±SD. Student's *t*-test and one-way analysis of variance (ANOVA) were applied to check significant differences in drug release from different formulations. Differences were considered to be statistically significant at $p<0.05$.

RESULTS AND DISCUSSION

Six different microcapsules formulations were prepared by solvent evaporation using different polymers ratio. Pure acetone did not dissolve Eudragit; however acetone with 2% water fitted the criterion well. Liquid paraffin was used as the dispersion media or external phase. Petroleum ether was used to clean the microparticles since it removes liquid paraffin without affecting the integrity of the microparticles.

Results are shown in Table 2. The drug content was found to be very high in all the cases probably due to polymer loss by adherence to the container as a result of viscous nature of slurry. The incorporation efficiency was found to be good in all formulations. Highest incorporation efficiency 96.48 % was found in batch of MC6. Entrapment efficiency increase with increase in the polymer concentration from the results it can be inferred that there is a proper distribution of Albendazole in the microcapsules and the deviation is within the acceptable limits. The arithmetic mean particle size of the formulations was determined by the optical microscope fitted with an ocular micrometer and stage micrometer.

Table 2: Characterization of Albendazole microcapsules.

Batch Code	% Yield	%Incorporation efficiency (%)	Mean particle size (µm)	% Drug content	Angle of repose	Bulk density	Tapped density	Hausner's Ratio
MC1	90±0.08	88.58±0.21	180±2.5	96	18.1	0.60	0.62	1.031
MC2	96±0.12	90.72±0.45	210±3.2	90	22.5	0.61	0.63	1.030
MC3	94±0.32	88.46±0.42	195±1.5	93	20.4	0.62	0.64	1.024
MC4	90±0.41	93.57±0.08	230±3.6	94	19.3	0.59	0.61	1.046
MC5	93±0.37	90.24±0.11	240±1.8	95	21.5	0.57	0.59	1.040
MC6	97±0.46	96.48±0.38	245±3.5	98	20.6	0.64	0.66	1.029

(Mean± S.D., n=4)

In general mean particle size of the microcapsules significantly increases with increase in polymer concentration due to high viscosity of medium at a higher polymer concentration resulting in enhanced interfacial tension and diminished shearing efficiency.

The angle of repose of microcapsule ranges from 18-22.5° (Table 2). The values of angles of repose indicate excellent flow properties. *In vitro* release studies were carried out by employing USP XXIII rotating basket method.

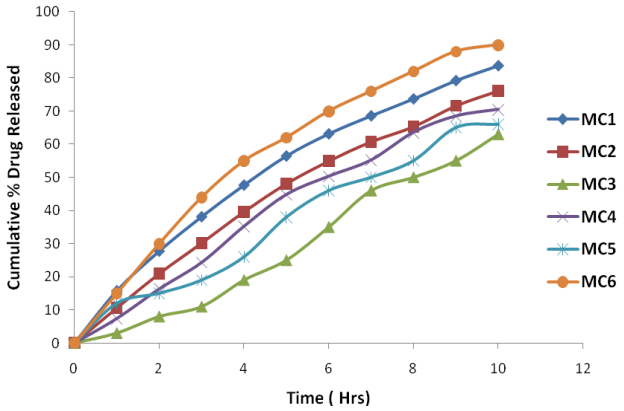

Figure 1: Comparative *in-vitro* release study of Albendazole microcapsules.

The release profile obtained for all the six formulations in 10 hrs. The release of drug from polymer matrix takes place after complete swelling of the polymer and as the amount of polymer in the formulation increases the time required to swell also increase thereby decrease in the drug release. However, the release showed a biphasic release with an initial burst effect. Maximum drug release was shown by microcapsules formulation of batch MC6 (90.18%) and minimum release is shown by formulation of batch MC3 (63.7%).

CONCLUSIONS

Different microcapsules formulations were prepared by solvent evaporation method using different polymers like Eudragit RS-100, chitosan and HPMC. From the results it seems that formulation MC6 was found to be satisfactory in terms of excellent micromeritic properties, yield of microcapsule, (97±0.46%), incorporation efficiency (96.48±0.38%) and highest *in vitro* drug release of 90.18%) % in a sustained manner with constant fashion over extended period of time for 10 hrs. Hence the prepared Albendazole microcapsules may prove to be potential candidate for safe and effective sustained drug delivery. Further *in-vivo* investigation is required to establish efficacy of these formulations.

AUTHOR'S CONTRIBUTION

Peter OI: writing original draft, methodology, investigation, formal analysis, data curation, conceptualization. **Ifeoma UC:** writing, review and editing, methodology, formal analysis, data curation, conceptualization. All the authors approved the finished version of the manuscript.

ACKNOWLEDGEMENTS

The authors extend their thanks and appreciation to the Nnamdi Azikiwe University Awka, Nigeria to provide necessary facilities for this work.

CONFLICT OF INTEREST

None to declare.

REFERENCES

1. Jantzen GM, Robinson JR, Sustained and controlled-release drug delivery systems, in modern pharmaceutics, Banker GS and Rhodes CT, eds. Informa healthcare: USA; 2009; 502.
2. Robinson JR, Lee VHL. Controlled drug delivery: Fundamentals and Applications. USA: informa healthcare. 2009; 20, 5-6.
3. Kothawade KB, Gattani SG, Surana SJ, Amrutkar JR. Colonic Delivery of Aceclofenac using combination of pH and time dependent polymers. Ind. Drugs 2009; 46 (11): 67-70.*https://doi.org/10.1081/DDC-120021315*

4. Chien YW. Novel drug delivery systems: oral drug delivery and delivery systems. New York: Marcel Dekker; 1992; 141. *https://doi.org/10.20959/wjpps20177-9607*
5. Guchelaar. Relative bioavailability of three newly developed albendazole formulations: a randomized crossover study with healthy volunteers. Antimicrob. Agents Chemother 2004; 48: 1051–1054; *https://doi.org/10.1128/AAC.48.3.1051-1054.2004*
6. García JJ, Bolas F, Torrado JJ. Bioavailability and efficacy characteristics of two different oral liquid formulations of albendazole. Int J Pharm 2003; 250: 351–358; *https://doi.org/10.1016/S0378-5173(02)00559-8*
7. Torrado S, Cadorniga R, Torrado JJ. Formulation parameters of albendazole solution. Int J Pharm 1996; 140: 45–50.*https://doi.org/10.1016/0378-5173(96)04545-0*
8. Lopez S, Torrado S, Torrado AR, Bolás F. Improvement of albendazole efficacy against enteral, but not against parenteral stages of *Trichinella spiralis* by preparing solid dispersions in polyvinyl pyrrolidone. Chemo Therap 1997; 43. *https://doi.org/10.1159/000239602*
9. Kalaiselvan R, Mohanta GP, Kannan K, Manna PK, Manavalan R. Optimization of drug-polymer mixing ratio in albendazole-polyvinylpyrrolidone solid dispersion by moisture absorption studies. Acta Pharm Sci 2006; 48, 141–151.*https://doi.org/10.1016/j.ejps.2018.07.027*
10. Allen LV, Popovich NG, Ansel HC. Ansel's pharmaceutical dosage forms and drug delivery systems. 9th ed. Lippincott Williams and Wilkins: USA. 2011; 258-259.
11. Waqas BS, Asad M, Nazir I, Qamar S. Alamgeer. Development and *in-vitro* evaluation of orlistat microcapsules by ionic gelation method. Europ J Bas App Sci 2016; 3 (3): 32-43.
12. Bogdansky S. Natural polymers as drug delivery systems, In: Biodegradable polymers as drug delivery systems, Mark Chasin and Robert Langer (eds.) New York: Marcel Dekker Inc, 231- 232. *https://doi.org/10.1146/annurev-chembioeng-073009-100847*
13. Bhanja S, Panigrahi BB, Shukla N, Hardel DK, Sudhakar M. Formulation and *in vitro* evaluation of nicardipine hydrochloride microcapsules. Asian J Pharm Clin Res 2012; 5(3): 60-63.
14. Jose S, Dhanya K, Cinu TA, Litty J, Chacko AJ. Colon targeted drug delivery: different approaches. J Young Pharm. 2009; 1: 13-19. *https://doi.org/10.5001/omj.2010.24*
15. Narkhede PS, Umarkar AR, Patil PP, Patil PV, Jain S. Formulation and evaluation of tetracycline hydrochloride microcapsules by solvent evaporation method. Int J Pharm Biol Sci 2011; 1(3): 372-376.
16. Prakash K, Raju PN, Shanta KK, Lakshmi MN. Preparation and characterization of Lamivudine microcapsules using varius cellulose polymers. Trop J Pharm Res 2007; 6(4): 841-847. *https://doi.org/10.4314/tjpr.v6i4.14668*