Available online on 10.01.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

Formulation and characterization of sustained released tablet of deflazacort for colon targeting

Patil Shubhangi*[1], Agrawal Ankit[2], Singh Gurdeep[1], Gupta M K[1]

[1]Department of Pharmaceutics, Oriental College of Pharmacy & Research, Oriental University, Indore, Madhya Pradesh, India

[2]Department of Pharmaceutics, Chameli Devi Institute of Pharmacy, Indore, Madhya Pradesh, India

ABSTRACT

Deflazacort is a glucocorticoid used as an anti-inflammatory and immunosuppressant. Deflazacort are commonly Prescribed for the patient in disease condition such as Inflammatory Bowel Disease (IBD) ulcerative colitis (UC) and Crohn's disease (CD). Delivery of drug substances to the ileo-colonic region may be an essential element of successful drug treatment (improved efficacy or reduced systemic toxicity) in topical treatment of the colon. The colon targeted drug delivery can also be used for effective treatment of diseases. This may improve efficacy of drug treatment, decrease in dose to be administered, improved drug utilization. It is a promising site for a drug which is unstable or poorly absorbed. Currently available formulation of deflazacort is conventional solid dosage form (6, 12, 18 & 30 mg tablets). Dosage form require frequent dose of administration due to its short half life of 1.1-1.9 hrs. So, present study is aimed to develop an colon targeted sustained release dosage form has been developed as these releases the drug slowly into the ileo- colonic region and maintain constant drug concentration in the serum for longer period of time.

Keywords: Deflazacort, Colon Targeting, IBD, Crohn's Disease

Article Info: Received 15 Oct 2018; Review Completed 25 Dec 2018; Accepted 28 Dec 2018; Available online 10 Jan 2019

Cite this article as:

Patil S, Agrawal A, Singh G, Gupta MK, Formulation and characterization of sustained released tablet of deflazacort for colon targeting, Journal of Drug Delivery and Therapeutics. 2018; 8(6-A):102-105

***Address for Correspondence:**

Ms. Shubhangi Patil, Research Scholar, Oriental College of Pharmacy & Research, Oriental University, Indore, Madhya Pradesh, India

INTRODUCTION

Oral controlled release dosage forms have been developed over the past three decades due to their considerable therapeutic advantages such as ease of administration, patient compliance and flexibility in formulation. Microsphere carrier systems made from the naturally occurring biodegradable polymers have attracted considerable attention for several years in sustained drug delivery. 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 [1-3]. They have varied applications and are prepared using assorted polymers[4]. However, the success of these microspheres is limited owing to their short residence time at the site of absorption. It would, therefore, be advantageous to have means for providing an intimate contact of the drug delivery system with the absorbing membranes[5] Ongoing research in the area of oral delivery of drugs, a discipline which has basked in the spotlight of pharmaceutical sciences for the past 70 years, has led to improved and profound insights into the physiology, biology and physical chemistry (pharmacokinetics, partitioning phenomenon) of organs, compartments, cells, membranes, cellular organelles and functional proteins (e.g. transporters) associated with absorption processes of drugs in the gastrointestinal tract (GIT). Deflazacort is a glucocorticoid used as an anti-inflammatory and immunosuppressant. Deflazacort are commonly Prescribed for the patient in disease condition such as Inflammatory Bowel Disease (IBD) ulcerative colitis (UC) and Crohn's disease (CD). The colon targeted drug delivery can also be used for effective treatment of diseases. This may improve efficacy of drug treatment, decrease in dose to be administered, improved drug utilization. It is a promising site for a drug which is unstable or poorly absorbed.[6, 7]

MATERIALS & METHODS

Method of Preparation of Core Tablet[8]

- Core tablet was prepared by Direct Compression method.
- Weighed accurate quantity of drug (Deflazacort) with polymers (HPMC K4M, Methocel K15M and Ethyl cellulose,) and other excipient (MCC PH-102) & talc.
- Then above directly compressible ingredient was passed through sieve no. 40# and mixed properly.

- Then the magnesium stearate and talc (100# passed) were mixed along the powder. Tablets were prepared by using eight station rotary tablet press.

Procedure for Tablet Coating[9]:

- The tablets were dip-coated with different concentration of Eudragit S100 dispersion in a mixture of acetone: isopropyl alcohol (1:1) containing 1.25% polyethylene glycol plasticizer. The weighed core tablets were dipped into coating solutions by holding with forceps and after dipping placed on a glass plate .The tablet were dried initially at room temperature for 15 min and then in a hot air oven at 60°C for 30 minutes.

Table 1: Various formulation of Deflazacort Tablet

Ingredient (mg.)	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11
Deflazacort	12.30	12.30	12.30	12.30	12.30	12.30	12.30	12.30	12.30	12.30	12.30
HPMC K4M	20	40	60	-	-	-	20	-	20	20	20
HPMCK15M	-	-	-	20	30	40	-	20	-	-	-
Ethyl cellulose	-	-	-	-	-	-	8	8	-	-	-
MCC PH 102	162.70	142.70	122.70	162.70	152.7	142.7	154.7	154.7	162.7	162.7	162.70
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium Stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total wt. (mg.)	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

Table 2: Ingredients of Coating Solution

Coating solution Composition			
	I	**II**	**III**
Eudragit S100	8%	10%	12%
PEG 400	1.25%	1.25%	1.25%
Acetone: Isopropyl alcohol (1:1)	20 ml	20 ml	20 ml

RESULT & DISCUSSION

Table: 03 Evaluation Parameters for (Uncoated Tablet) F_1-F_9 Optimized formulation

Batch Code	Hardness (kg/cm²)	Thickness (mm)	% Friability	Drug Content Uniformity (%)	Average Weight of Tablet (mg)
F1	5.83±0.5	3.1±0.2	0.55	96.58	202±2.00
F2	5.24±0.5	3.0±0.2	0.61	95.51	200±2.16
F3	5.05±0.5	3.0±0.2	0.65	96.78	204.23±1.77
F4	5.64±0.5	3.1±0.3	0.59	94.36	202.15±2.20
F5	6.01±0.5	3.2±0.3	0.63	95.72	204±1.20
F6	5.93±0.5	3.1±0.3	0.66	97.34	200±2.05
F7	5.32±0.5	3.1±0.2	0.7	94.56	203.25±1.47
F8	6.25±0.5	3.0±0.3	0.74	96.89	201.14±0.51
F9	6.06±0.5	3.1±0.2	0.78	95.62	200.16±0.53

Post- Compression parameter for uncoated tablet is tested for hardness, thickness, friability, drug content, weight variation. Hardness of the prepared tablets was found in range of 5.5-6.5 kg/cm². Drug content is come under 90-110% in range as specified in pharmacopoeia[10]. All the tablet formulations showed acceptable pharmacopoeia limits and complied with the in-house specifications for thickness, weight variation, drug content, hardness, and friability.[11, 12]

Table 4: Evaluation Parameters for Factorial Batches of (Coated Tablets) F_1-F_9 Optimized formulation

Batch Code	Hardness (kg/cm²)	Thickness (mm)	Average Weight of Tablet (mg)	% Weight Gain	%Swelling study
F1	6.73±0.5	4.14±0.2	218±1.24	9.19±0.52	180
F2	6.74±0.5	4.05±0.2	217±2.16	8.91±0.54	210
F3	6.64±0.5	4.17±0.2	219.25±0.82	9.14±0.18	230
F4	6.84±0.5	4.18±0.3	218.35±1.75	9.52±0.48	165
F5	6.66±0.5	4.21±0.3	217.25±0.42	9.18±0.57	198
F6	6.7±0.5	4.2±0.3	218.14±2.00	9.64±0.53	222
F7	6.5±0.5	4.15±0.2	217.23±1.77	9.84±0.62	152
F8	6.49±0.5	4.2±0.3	218.15±2.20	9.58±0.48	185
F9	6.58±0.5	4.12±0.3	218.15±2.20	9.95±0.48	195

From trial batches B_1-B_8 in Vitro drug release studies are shown in table no.5. Batch B_1-B_3 in which HPMC K4M are used as hydrophilic polymer as it shows it release drug initially before 10 hours. HPMC K15M is also used in which batch B_4-B_6 shows 80-88% drug release. So, it's better to prepare combination batches B_7-B_8 in which HPMC K4M combined with hydrophobic polymer such as ethyl cellulose to retard the drug release as a result batch B_7 shows 93.13% drug release in 10 hours.[13-14]

Table: 05 % Cumulative Drug Release profile of various Formulations

Time (Hrs.)	% Cumulative Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0
6	28.75	21.38	17.58	26.91	19.56	16.67	24.76	18.81	15.86
7	43.02	32.35	29.36	37.7	32.44	25.76	33.15	30.96	22.63
8	52.12	44.65	42.3	44.43	43.64	36.33	41.52	42.05	26.11
9	66.58	53.78	51.66	53.52	51.25	44.54	49.6	51.28	37.26
10	71.22	60.65	59.7	60.26	62.23	55.12	57.63	60.25	45.26
11	77.36	68.23	67.68	68.32	70.63	63.45	65.22	66.52	51.88
12	82.05	74.52	75.74	73.79	76.95	72.7	74.52	71.23	59.89
13	86.54	82.74	81.85	80.74	82.5	80.52	82.15	78.52	64.76
14	91.04	88.92	87.32	86.26	88.74	86.44	87.32	84.23	76.26
15	95.12	94.72	93.16	94.26	92.48	90.56	91.13	88.12	85.57

CONCLUSION

Deflazacort is a glucocorticoid. Its anti-inflammatory and immunosuppressive effects are used in treating various diseases and are comparable to other anti-inflammatory steroids.

A 3^2 full factorial design was used to check effect of HPMC K4M and Ethyl cellulose on tablet characteristics. %CDR at 6 hours (Q_6) and %CDR at 6 hours (Q_{15}) selected as dependent variables. Multiple linear regression analysis and ANOVA results showed that selected factors were significant as p value was lower than 0.05. Full model and reduced model for individual factor were prepared and evolved. Check point batches was prepared and the results of actual value were comparable with predicted value.

The release profile of the selected formulation was found to follow Higuchi model (r^2 =0.9984). Further, selected formulation (Batch F_4) was subjected to short term accelerated stability study at 60±2°C / 75±5 % RH after packing in Aluminium foil; similarity factor was found to be 85%,results revealed that applied storage conditions showed no significant effect on drug content, hardness in vitro drug release profile after storage for two weeks.

REFERENCES

1. Woo BH, Jiang G, Jo YW, Deluca PP. Preparation and characterization of a composite PLGA and poly (acryloylhydroxyl methyl starch) microsphere system for protein delivery. Pharm Res, 2001; 18:1600-1606.
2. Capan Y, Jiang G, Giovagnoli S, Deluca PP. Preparation and characterization of Poly (D, L-lactide –co-glycolide) microspheres for controlled release of human growth hormone. AAPS Pharm Sci Tech, 2003; 4: E28.
3. Gohel MC, Amin AF. Formulation and optimization of controlled release Diclofenac sodium microspheres using factorial design. J control release, 1998; 51:115-122.
4. Vasir JK, Tamwekar K, Garg S. Bioadhesive microspheres as a controlled drug delivery system. Int J Pharm, 2003; 255:13-32.
5. 5. Ikeda K, Murata K, Kobayashi M, Noda K. Enhancement of bioavailability of Dopaminevia nasal route in beagle dogs. Chem. Pharm Bull (Tokyo), 1992; 40:2155-2158.
6. Das M and Ghosh L. Evaluation of Polymers for Compression Coating of 5-Aminosalicylic Acid Matrix Tablets For Colon Targeting, International Journal of Pharmacy and Pharmaceutical Sciences, 2013; 5(3):122-125.
7. Dev RK, Bali V and Pathak K. Novel microbially triggered colon specific delivery system of 5-Fluorouracil: Statistical optimization, in vitro, in vivo, cytotoxic and stability assessment, International Journal of Pharmaceutics, 2011; 4 (11):142–151.
8. Khan ZM, Prebeg ZE and Kurjakovic N. A pH-dependent colon targeted oral drug delivery system using methacrylic acid copolymers I. Manipulation of drug release using EudragitÒ L100-55 and EudragitÒ S100 combinations: Journal of Controlled Release, 1999; (58):215–222.
9. Ahrabi SF, Madsen G, Dyrstad K, Sande SA and Graffner C, Development of pectin matrix tablets for colonic delivery of model drug ropivacaine: European Journal of Pharmaceutical Sciences, 2000; 10:43–52.
10. Sahib MN, Abdulameer SA and Rasool AA, Design and In Vitro Evaluation Of Prednisolone Tablets As A Potential Colon Delivery System: Asian Journal of Pharmaceutical and Clinical Research, 2009; 2(4):84-93.
11. Pundir S, Badola A and Sharma D., Sustained Release Matrix Technology and Recent Advance in Matrix Drug Delivery System: A Review: International Journal of Drug Research and Technology, 2013; 3(1):12-20.
12. Rao NG, Prasanna KR, Nayak BS. Review on Matrix Tablet as Sustained Release: International Journal of Pharmaceutical Research & Allied Sciences, 2013; 2(3):1-17.
13. Sharma PR and Lewis SA, Design and in vitro/in vivo evaluation of extended release matrix tablets of nateglinide: Journal of Young Pharmacists, 2013; (5):167-172.
14. Patel MV, Parmar ND, Bagda AN, Singh SK and Patel S. Formulation and Evaluation of Lornoxicam Matrix Tablets by Using Hydrophilic and Hydrophobic Polymer, 2012; 1(3):87-92.
15. Chellakumari Daisy, Selvapriya A., Soniya C, Dinesh Kumar A. Formulation and Evaluation of Deflazacort Loaded Gelatin Microspheres; International Journal of Pharmacy and Biological Sciences, 2017; 7:8-13.