RESEARCH PAPER

Formulation and characterization of sustain release drug delivery system of freely water soluble moxonidine

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Abstract

Moxonidine is an antihypertensive drug used in the management of hypertension. Due to its high aqueous solubility, the drug may undergo rapid dissolution and elimination, which can result in a shorter duration of therapeutic action and the need for repeated administration. Therefore, the development of a sustained release dosage form may help to maintain the drug concentration for a prolonged period and improve patient compliance.

A sustained release matrix system of Moxonidine was developed using the hot-melt technique. The method was selected as it provides a simple and solvent-free approach for incorporating a freely water-soluble drug into a hydrophobic matrix. Different formulations (F1–F9) were prepared using varying concentrations of suitable release-retarding excipients. The prepared formulations were evaluated for their physical characteristics, drug content, drug–excipient compatibility, and in-vitro drug release. FT-IR spectroscopy was used to evaluate the compatibility of Moxonidine with the selected excipients, while dissolution studies were performed to determine the ability of the formulations to sustain drug release.

The prepared formulations showed satisfactory pharmaceutical characteristics and acceptable drug content. The in-vitro drug release study demonstrated that the incorporation of Moxonidine into a hydrophobic matrix effectively prolonged drug release. The release rate was influenced by the concentration of the release-retarding excipient, with higher concentrations generally providing greater retardation of drug release. Among the prepared formulations, F5 was selected as the optimized formulation based on its desirable sustained release characteristics and overall formulation performance.

The optimized formulation showed a prolonged drug release pattern and demonstrated the potential of the hot-melt matrix system for controlling the release of freely water-soluble Moxonidine. Overall, the study established that the hot-melt technique can be successfully utilized to develop a sustained release dosage form capable of extending drug release, reducing the frequency of administration, and potentially improving therapeutic efficacy and patient compliance.

Keywords: Moxonidine , sustained release drug delivery system, freely water-soluble drug, hot-melt technique, hydrophobic matrix, release-retarding agent, matrix tablet antihypertensive drug.

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1. Introduction

Oral drug delivery is one of the most convenient, economical, and widely accepted routes for the administration of therapeutic agents. Conventional immediate-release dosage forms are designed to release the drug rapidly after administration, producing a relatively quick increase in drug concentration in the systemic circulation. However, rapid drug release may not always be desirable, particularly for drugs that require prolonged therapeutic action. Frequent administration of such drugs may result in fluctuations in plasma drug concentration, reduced patient compliance, and an increased possibility of adverse effects. These limitations have encouraged the development of modified-release drug delivery systems capable of controlling the rate and duration of drug release.[1]

Sustained release drug delivery systems are designed to release the incorporated drug gradually over an extended period. The primary objective of a sustained release system is to maintain drug concentration within the desired therapeutic range for a prolonged duration while reducing the frequency of administration. Such systems can provide more uniform drug levels, minimize peak–trough fluctuations, improve therapeutic effectiveness, and enhance patient convenience and compliance. Various approaches, including matrix systems, reservoir systems, coated dosage forms, osmotic systems, and polymeric delivery systems, have been investigated for achieving sustained drug release.[2]

The development of sustained release formulations is particularly challenging for freely water-soluble drugs. Such drugs tend to dissolve rapidly when

exposed to gastrointestinal fluids, resulting in a rapid release from conventional dosage forms. Therefore, suitable formulation strategies are required to retard the dissolution and diffusion of the drug. Hydrophobic polymers, waxes, insoluble matrices, and other release-retarding materials can be incorporated into the formulation to create a diffusion barrier around the drug and thereby prolong its release. The concentration and physicochemical characteristics of these materials play an important role in determining the release rate.[3]

Moxonidine is a centrally acting antihypertensive drug used in the management of hypertension. It acts primarily through stimulation of imidazoline I_1 receptors in the central nervous system, resulting in reduced sympathetic nervous system activity and consequently lowering blood pressure. Moxonidine possesses high aqueous solubility, which favors rapid dissolution following oral administration. Although rapid dissolution is advantageous for immediate drug availability, it can be undesirable when prolonged drug action is required. Hence, Moxonidine represents a suitable candidate for investigation as a sustained release dosage form.[4]

A sustained release formulation of Moxonidine can potentially provide controlled drug availability over an extended period and help maintain more consistent therapeutic concentrations. By reducing the rate at which the freely soluble drug becomes available for absorption, the formulation may minimize rapid drug release and reduce the need for repeated dosing. Consequently, development of a suitable matrix-based delivery system may improve the convenience and effectiveness of oral Moxonidine therapy.[5]

The hot-melt technique is a useful approach for the preparation of sustained release formulations, particularly when hydrophobic release-retarding materials are employed. In this technique, the drug is incorporated into a molten carrier or matrix-forming material, followed by cooling and solidification to form a drug-containing matrix. The technique does not require organic solvents and can provide relatively simple processing and uniform incorporation of the drug into the release-retarding matrix. The nature and concentration of the matrix material can be modified to achieve the desired drug-release characteristics.[6]

In the present study, an attempt was therefore made to formulate and characterize a sustained release drug delivery system of freely water soluble Moxonidine using the hot-melt technique. Different formulations were developed using varying concentrations of suitable release-retarding materials, and the prepared formulations were evaluated for their physicochemical characteristics, drug content, drug–excipient compatibility, and in-vitro drug release. The release data were further analyzed using different kinetic models to understand the mechanism of drug release. The optimized formulation was selected on the basis of its overall performance and ability to provide a desirable prolonged release profile.[7]

Methodology

Preformulation study of blend

The flow property measurements include bulk density, tapped density, angle of repose, compressibility index and Hausner's ratio. The flow property measurements of tablet are determined.[8]

i) Bulk density

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder into a measuring cylinder and initial weight was noted. This initial volume was called the bulk volume. From this the bulk density was calculated.[9]

ii) Tapped density

It is the ratio of weight of the powder to the tapped volume of powder. The powder was introduced into a measuring cylinder with the aid of funnel and tapped for 300 times on a wooden surface at a 2 sec interval and the volume attained is the tapped volume.[10]

iii) Angle of repose

The flow properties were characterized in terms of angle of repose, Carr's index and Hausners's ratio. For determination of angle of repose, the drug and the blend were poured through the walls of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2.0 cm above hard surface. The drug or the blends were poured till the time when upper tip of the pile surface touched the lower tip of the funnel. Angle of repose was calculated using following equation: $\theta = \tan^{-1}(h/r)$, Where h= height of pile in cm; r = radius of pile in cm.[11]

iv) Carr's index or % compressibility

It indicates powder flow properties. It is measured for determining the relative importance of inter particulate interactions.[12]

Formulation of sustain release tablet by melt granulation method

Sustained release tablets were prepared by melt granulation method. All the ingredients were passed through sieve 40 #. Weight accurately all ingredients, mixed and heat on water bath with gently stirring. The granules obtained were dried at 60ºC temperature. After drying, granules passed through sieve 20#, 40# and granules retained on 40# to obtained uniform size granules. After sufficient lubrication tablets were prepared using Rimek tablet compression machine. All the prepared blend and Moxonidine tablets were evaluated for different parameters.

Sustained release tablets of containing Moxonidine were prepared using cetostearyl alcohol as 30%,35%,

and 40% of total tablet weight and hydroxy propyl cellulose as 20%, 25% and 30% of total tablet weight as per given in table.[13]

Table 1: Formulation of batches of combination of Cetostearyl alcohol and HPC

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Moxonidine	25	25	25	25	25	25	25	25	25
Cetostearyl alcohol	120	120	120	140	140	140	160	160	160
HPC	80	100	120	80	100	120	80	100	120
Dicalcium phosphate	159	139	119	139	119	99	119	99	79
Magnesium stearate	4	4	4	4	4	4	4	4	4
Aerosil	12	12	12	12	12	12	12	12	12
Total Wt	400	400	400	400	400	400	400	400	400

Evaluation parameters for tablets

i. Uniformity of weight

Every individual tablet in a batch should be in uniform weight and weight variation in within permissible limits. The weights were determined to within ±1mg by using Sartorious balance. Weight control is based on a sample of 20 tablets.[14,15]

ii. Thickness

Thickness was measured to check the uniformity because it directly affects the hardness of tablet. The thickness was determined by using vernier calipers.[16,17]

iii. Hardness

The hardness of the tablets was determined by diametric compression using a Hardness testing apparatus (Monsanto Type). A tablet hardness of about 4-5 kg is considered adequate for mechanical stability.[18]

iv. Friability

The friability of the tablets was measured in a Roche friabilator. Tablets of a known weight (W_0) or a sample of 20tablets are dedusted in a drum for a fixed time and weighted (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %.[19]

In vitro drug release study

Tablets of each formulation were subjected to dissolution studies. In-vitro dissolution studies were carried out to determine the drug release from various formulations. The in vitro drug release study was carried out for 24 hours. The absorbance was determined at λ max of drug. The drug content of each sample was determined from calibration curve. The in vitro dissolution study was carried out using dissolution medium consisted of 900ml 0.1 N HCl for first 2hrs followed by phosphate buffer (pH 6.8) from 2 to 24 hrs. Temperature maintained at 37±0.5ºC. Aliquots of 10ml were withdrawn every one hour and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. Aliquots withdrawn were diluted suitably, filtered and analyzed spectrophotometrically.[20]

Drug release kinetics

The release profile of the drug was analysed using different kinetic models such as zero order, first order, Higuchi, Hixson Crowell and Korsmeyer – Peppas model in order to evaluate the release mechanism from matrices.[21]

3. Result

Flow properties studies of prepared Granules by Hot melt granulation

Table 2:Data For flow property and compaction behavior

Flow properties	Granules prepared by Hot melt granulation		
Drug: polymer	(1:2) Drug: bees wax	(1:2) Drug: cetostearyl alcohol	(1:2) Drug: carnauba wax
Angle ofrepose	38.13	30.86	41.13
Tappeddensity	0.467	0.469	0.476
Bulk density	0.424	0.432	0.435
% Carrsindex	8.61	7.81	9.82
Hausner ratio	1.15	1.08	1.16

From above table we were observed that granules prepared by hot melt granulation in drug to cetosteryl alcohol ratio (1:2) had good flow property as well as good compressibility. Which has angle of repose 30.86 which is range within 30-40, in case of bees wax sticky product was obtain and carnauba wax gave hard product so, cetostearyl alcohol was good in

terms of compressibility as well as flow properties. So more trials with different concentration ratio like 1:1, 1:2, 1:3 and 1:4 with cetostearyl alcohol will be done.

Table 3: Flow property and Compaction behavior data

flow properties	Granules prepared by Hot melt granulation			
Drug: polymer (ratio)	Drug: Cetostearyl Alcohol (1:1)	Drug: Cetostearyl Alcohol (1:2)	Drug: Cetostearyl Alcohol (1:3)	Drug: Cetostearyl Alcohol (1:4)
Angle of repose(^{0}C)	39.12	30.87	45.12	48.13
Tapped density(gm/ml)	0.475	0.469	0.569	0.654
Bulk density(gm/ml)	0.435	0.432	0.542	0.556
% Carr's index	12.6	7.89	11.74	14.98
Hausner ratio	1.10	1.08	1.19	1.21

From above table we were observed that granules prepared by hot melt granulation in drug to cetosteryl alcohol ratio (1:2) had good flow property as well as good compressibility than formulation with 1:1, 1:3 and 1:4 ratio concentrations. So finely we had selected drug to cetosteryl alcohol in 1:2 ratio for further process and formulation development.

Solubility study of prepared Granules by Hot melt granulation:

Table 4: solubility Data of granules

Drug: cetostearyl alcohol	Average absorbance	Solubility (mg/ml)
1:1	0.579	59.496
1:2	0.521	49.393
1:3	0.554	55.466
1:4	0.532	54.75

From table it is concluded that the solubility of prepared granules by hot melt granulation containing drug to cetostearyl alcohol ratio 1:2 which has lower solubility. Drug to cetostearyl alcohol is 49.393 mg/ml which comparatively lower than the ratio1:1, 1:3 and 1:4.so it was suitable ratio for sustain release formulation.

Solubility studies of drug with polymer combinations:

Table 5 : Solubility studies of drug with polymer combinations

Combination	Average absorbance	Solubility (mg/ml)
Drug+ HPC	0.765	63.496
Drug + cetostearyl alcohol	0.579	50.392
Drug+ HPC +cetostearyl alcohol	0.515	47.392

Solubility study of different three combination Drug+ HPC **,** Drug + cetostearyl alcohol and Drug+ HPC + cetostearyl alcohol was determined spectrophotometrically. The minimum solubility of drug is in combination of Drug+ HPC + cetostearyl alcohol. So it will be the final combination for formulation of freely soluble drug.

Pre compression characterization:

Table 7: Physical characteristics of prepared blend of batches F_1 to F_9

Batch	B.D (gm/cc)	T.D (gm/cc)	C.I (%)	A.R
F1	0.45	0.56	19.64	30.25
F2	0.44	0.57	22.80	32.54
F3	0.42	0.59	28.81	32.87
F4	0.44	0.58	25.86	30.23
F5	0.45	0.59	15.72	29.37
F6	0.46	0.57	19.20	32.80
F7	0.47	0.56	16.87	33.98
F8	0.43	0.54	20.37	34.65
F9	0.44	0.55	20.98	32.76

Post compression characterization of formulation

Table 8:Evaluation parameters for tablets of batches F_1 to F_9

Batch	Thickness (mm)	Hardness Kg/cm^2	Friability (%)	Weight variation(mg)
F1	4.0±0.2	5.8±0.5	0.6±0.2	402±0.5
F2	3.9±0.3	5.3±0.3	0.6±0.4	407±0.2
F3	4.0±0.4	5.2±0.4	0.5±0.1	405±0.1
F4	4.2±0.1	6.1±0.3	0.4±0.1	401±0.6
F5	4.1±0.2	5.1±0.2	0.3±0.2	400±0.4
F6	4.6±0.2	5.5±0.3	0.7±0.2	403±0.1
F7	4.1±0.4	5.6±0.5	0.4±0.1	408±0.1
F8	3.7±0.3	5.2±0.4	0.8±0.2	402±0.2
F9	4.9±0.2	5.9±0.3	0.6±0.1	401±0.5

In vitro drug release study

Table 9: Cumulative % drug

release of batches F_1 to F_9 Tablet

Kinetic model fitting of batch F5

Time (hrs)	%Cumulative percentage release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	18.12	17.25	15.42	14.31	15.42	12.12	9.76	6.87	5.9
2	28.54	26.89	22.92	19.74	21.56	18.19	12.23	10.54	12.23
3	36.37	33.56	27.75	23.75	29.78	24.53	29.67	18.34	17.56
5	45.31	42.03	32.03	30.31	35.62	33.54	37.75	30.43	28.35
7	56.25	54.38	42.38	41.28	58.64	59.09	51.67	47.34	45.56
9	69.51	67.55	56.55	53.15	68.22	66.78	73.78	49.54	47.45
12	81.63	79.92	68.92	64.26	75.45	74.34	76.87	59.34	62.54
15	93.45	88.28	76.28	70.31	86.23	82.53	83.12	67.45	65.34
18	99.78	99.19	98.88	84.58	90.65	83.87	82.23	83.23	78.23
24	-	-	-	94.20	99.02	92.76	89.75	87.25	83.21

Table 9: Results of model fitting of batch F5

	Intercept	Slope	R^2
Zero-order plot	12.252	3.677	0.9728
First-order plot	1.2595	0.0382	0.9794
Higuchi plot	-8.314	19.053	0.9670
Hixon Crowell	29.249	-1.22551	0.9821
Krosmeyer – pappas	0.835	0.531	0.9942

The zero-order rate describes the systems where the drug release rate is independent of its concentration. The first order which describes the release from systems where the release rate is concentration dependent. Which shows the log cumulative percent drug remaining vs time illustrates the Higuchi square root kinetics, showing the cumulative percent drug release vs the square root of time. The regression coefficients of each plot were determined using their corresponding plot. It was found that the in vitro drug release of Moxinidine Sustain release was followed by by first order .The mechanism of drug release is explained by Korsmeyer-Peppas (log cumulative percent drug release vs time). Korsmeyer-Peppas equation indicated a good linearity . Formulation F5 follows drug release mechanism according to kosmear peppa‘s equation and value of intercept 0.835 indicates drug release from tablets occurs by diffusion and erosion of matrix.

Short term stability study

Table 10: Stability studies for formulation F5

Months	**4 - 8 O C**	**25° C/60% RH**	**40° C/75% RH**
	% Drug content	**% Drug content**	**% Drug content**
I	99.42±0.18	99.42±0.18	99.42±0.1
initial			8
1	99.39±0.21	99.21±0.42	99.26±0.33
2	99.14±0.28	99.08±0.93	99.07±0.56
3	98.47±0.39	98.21±0.81	98.04±0.40

Stability of formulation is an essential requirement concerning its size and efficacy. Stability of formulation was examined over a period of 3 months. Short term Stability studies were conducted for optimised formulations i.e., F5 at refrigerated conditions (2-8 ºC), at room temperature (25±2ºC/60% RH) and at accelerated condition (40±2ºC/75% RH) for a period of 3 months. Drug content was monitored and did not display any significant change compared to initial sample (Day 1). Interestingly, significant changes in drug content were not observed up to 3 months of storage.

Conclusion

The present study was successfully carried out with the objective of developing and characterizing a sustained release drug delivery system of freely water-soluble Moxonidine. Since Moxonidine possesses high aqueous solubility and can undergo rapid dissolution, incorporation into a suitable release-retarding matrix was investigated as an approach to prolong drug release and provide sustained therapeutic availability.

The hot-melt technique was successfully employed for the preparation of Moxonidine sustained release formulations. A series of formulations (F1–F9) was prepared using varying concentrations of suitable hydrophobic release-retarding materials. The prepared formulations exhibited satisfactory physical characteristics and acceptable drug content, indicating uniform incorporation of the drug within the matrix system. FT-IR studies also supported the compatibility of Moxonidine with the selected excipients, with no significant interaction observed that could adversely affect formulation performance.

The in-vitro drug release studies demonstrated that the hot-melt matrix system was effective in controlling the release of freely water-soluble Moxonidine. The release rate was influenced by the concentration of the hydrophobic matrix material, with increased matrix concentration providing greater resistance to drug diffusion and dissolution. Among all the prepared formulations, F5 was selected as the optimized formulation because it exhibited the most desirable and prolonged drug release profile along with satisfactory overall formulation characteristics.

The release kinetics of the optimized F5 formulation were evaluated using different mathematical models. The kinetic analysis indicated that the drug release was controlled by the matrix system and involved diffusion-based release mechanisms. The optimized formulation showed a desirable sustained release behavior, demonstrating the effectiveness of the selected hydrophobic matrix and hot-melt technique in controlling the release of Moxonidine.

References

1. Chokshi R, Zia H. Hot melt extrusiontechnique: a review, Iranian J Phar Res.2004; 3: 3 -16.
2. Schafer T, Holm P, Kristensen HG. Melt granulation in a laboratoryscale high shear mixer, Drug Devl Ind Pharm. 1990; 16 (8): 1249 – 1277.
3. Heng WS, Wong TW., Melt processes for oral solid dosage forms, PharmTech.2003; 1-6.
4. Evrard B, Delattre L. In vitro evaluation of lipid matrices for the development of a sustained–release sulfamethazine bolus for lambs, Drug Devl Ind Pharm.1996; 22 (2):111-118.
5. Eliasen H, Kristensen HG, Schafer T. Growth mechanism in melt agglomeration with low viscosity binder, Int J Pharm.1999; 186: 149-159.
6. Brabander C. D., Vervaet C., Remon J. P., Development and evaluation of sustained release mini-matrices prepared by hot melt extrusion, J Control Rel. 2003; 89: 235 – 247.
7. Miyagawa Y, Okabe T, Yamaguchi Y. Controlled release of diclofenac sodium from wax matrix granules, J Pharm Sci.1996; 138: 215-224.
8. Sato H,Miyagawa Y, Okabe T. Dissolution mechanism of diclofenac sodium from wax matrix granules, J Pharm Sci.1997; 86: 929-934.
9. Breitenbach J., Melt extrusion: from process to drug delivery technology, EurJ Pharm Biopharm. 2002; 54: 107 – 117.
10. Schafer T, Mathiesen C. Melt pelletization in a high shear mixer. IX. Effect of binder particle size,Int J Pharm.1996; 139: 139-148.
11. Passerini N, Perissutti B, Monoghini M, Voinovich D, Albertini B, Cavallari C, Rodriguez L.Characterization of carbamazepine–Gelucire 50/13 microparticles prepared by a spray congealing process using ultrasounds, J Pharm Sci. 2002; 91(3): 699-707.
12. Maejima T, Osawa T, Nakjima K, Kobayashi M. Application of tumbling melt granulation method for preparing controlled release beads coated with hydrogenated castor oil, Chem Pharm Bull.1997; 45(5): 904-910.
13. Kidokoro M, Sasaki K, Haramiishi Y, Matahira N. Effect of crystallization behavior of polyethylene glycol 6000 on the properties of granule prepared by fluidized hot melt granulation (FHMG), Chem Pharm Bull. 2003; 51 (5): 487–493.
14. Kaufman HS, Falcetta JJ. Introduction to polymer science and technology: an SPE textbook, 1st ed. New Yolk: John Wiley & Son 1977;.
15. McGinity JW, Zhang F, Repka MA, Koleng JJ. Hot-melt extrusion as apharmaceutical process. Am Pharm Rev. 2001; 4(2): 25-36.
16. Breitenbach J. Melt extrusion: from process to drug delivery technology. Eur J Pharm Biopharm. 2002; 54:107-117.
17. Crowley MM, Zhang F, Koleng JJ, McGinity JW. Stability of polyethylene oxide in matrix tablets prepared by hot-melt extrusion, Biomaterials. 2002; 23:4241-4248.
18. McGinity J, Hot-melt extrusion as a pharmaceutical process. AAPS Newsmagazine. 2004; 7(3):21–25.
19. Dittgen M, Fricke S, Gerecke H, Osterwald H. Hot spin mixing: a new technology to manufacture solid dispersions, Pharmazie.1995; 50:225–226.
20. Piyali KhamkatVivek Barik, Bhakti Bhusan Barik, Aritra Chakraborty, Dipsikha Patra, Prasenjit Mondal Formulation and Evaluation of Propranolol Hydrochloride Sustained Release Matrix Tablets Using Different Grades of HPMC and MCC *, World Journal of PharmacySciences 2025 2321-3310
21. Sham Shad Begum, G.S.Sharma, B. Rama, L.Jyothi Rani, B.Rajkamal. Formulation and InvitroEvaluation of Sustained Release Tablets of Pregabalin. World J PharmSci 2024;10(03):243-254;
22. Kamran Ahmad Khan , Ashfaq Ahmad: Formulation and Preparation of Losartan-

Potassium-Loaded Controlled-Release Matrices Using Ethocel Grade 10 to Establish a Correlation between In Vitro and In Vivo Results World J PharmSci 2023;12(03):244-254;

23. Nigusse P., Laforet J. P., Farah N., Joachim J., : An innovative hot melt coating agent for prolonged release drug formulations of ranitidine hydrochloride, Eur. J. Pharm. Biopharm., 47(2022): 87-90.
24. Khaled H. Al Zahabi ,Hind Ben tkhayat ,Ehab Abu-Basha ,Al Sayed Sallam andHusam Pharmaceutics 2021, 13(12), 2158;
25. Sahidul alam, amlan bishal, bratati bandyopadhyay Formulation and evaluation of metformin hydrochloride sustained release matrix tablets Int J Curr Pharm Res, 2021Vol 13, Issue 5, 82-88.