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Optimization and Formulation Meloxicam-β-Cyclodextrin Orally Disintegrating Tablet Using Superdisintegrant Combination and Microcrystalline Cellulose as Filler-Binder

Fuad Soegibudiono Wiradjaja[1], Teuku Nanda Saifullah Sulaiman[1*], Abdul Rohman[1,2]
[1]Faculty of Pharmacy, Gadjah Mada University, Yogyakarta 55281 Indonesia
[2]Research Center of Halal Products, Gadjah Mada University, Yogyakarta 55281 Indonesia.
***Corresponding author: E-Mail: tn_saifullah@ugm.ac.id**

ABSTRACT

The aim of this study was to optimize and formulate orally disintegrating tablet of meloxicam (MLX) after its complexation with β-cyclodextrin and to investigate the effect of combination of croscarmellose sodium and crospovidone as superdisintegrants with microcrystalline cellulose as filler-binder on physical properties of tablet and dissolution of MLX. Inclusion complexes was prepared by spray drying then compressed in the form of tablets utilizing direct compression technique. Tablets were evaluated for the physical properties including weight uniformity, hardness, and disintegration time, wetting time, friability and content uniformity. Dissolution of MLX in 3 min were also analysed. All responses above were considered as responses in a D-optimal experimental plan. All results then analyzed with Design Expert® 7.1.5 to obtained optimum formula. Optimum area were observed with in 2.00 - 4.11% croscarmellose sodium, 4.11 – 5.00% crospovidone, and microcrystalline cellulose in 51.78 - 53.00%. The selected optimum formula was obtained in proportion of 2.53% croscarmellose sodium, 5.00% crospovidone, and 52.47% microcrystalline cellulose. It disintegrate in the oral cavity within 9 second and released more than 80% of MLX in 3 minute.

KEY WORDS: Meloxicam, β-cyclodextrin, Croscarmellose sodium, Crospovidone Microcrystalline cellulose.

1. INTRODUCTION

Orally disintegrating tablet (ODT) were defined as solid dosage forms containing medical substances which rapidly disintegrate usually in the matter of seconds when placed upon the tongue (FDA, 2008). Active ingredients then dissolve with the presence of saliva. Fast disintegration rate result in faster onset of action compared with conventional tablet dosage form. Moreover, keratineless mucose layer in oral cavity allows pregastric absorption which results in improved bioavailability (Kundu, 2008; Saurabh, 2012). ODT offer an advantage for patiens who have difficulty in swallowing, such as dysphagia, stroke, which is common among geriatric or pediatric population. ODT also be a first choice for traveler patient which access to water is limited (Deepak, 2012; Gupta, 2012).

Meloxicam is an oxicam derivate belongs to non steroid anti inflammatory drugs (NSAID) which seletively inhibite cyclo-oxygenase-2 (COX-2). Meloxicam used as first line therapy in the short-term management of rheumatoid arthritis and symptomatic therapy in acute exacerbation of ostheoarthritis (APA, 2012; Sweetman, 2009). Development of MLX oral dosage form has its own problem, due to its poor water solubility and it bitter taste (Sweetman, 2009; Moffat, 2011). Several techniques have been used to improve the solubility and dissolution characteristics of meloxicam, mainly by its complexation with cyclodextrins (Abdoh, 2007; Obaidat, 2008).

The basic principles in the development of ODT are the use of superdisintegrants to promote rapid disintegration of the tablet in oral cavity (Obaidat, 2007). Direct compression method is the most commonly used method in producing ODT because it's cost effectiveness among another methods. This method allows use of conventional instrument and offers limited number of processing steps, reduced process time, and utilizes commonly available excipients (Segale, 2007). As a conventional tablets, ODT formula generally contains filler-binder, superdisintegrant, lubricant, and taste masking agent. Disintegrant plays the most important role to produce fast disintegration (Tanuwijaya, 2013).

Several studies have shown that ODT formulated with different superdisintegrants may produce different physical characteristics of tablets. Upare (2012), reported the use of different superdisintegrants results in different characteristics of ODT, especially in the result of disintegration time and drug dissolution. Similar results were also reported by Battu (2007), Kulkarni (2011), Setty (2008).

Some previous study reported that used of combination of superdisintegrant results in better physical properties of ODT compared with single use of super disintegrant. Thulluru (2012), reported combination of superdisintegrants in ODT formulations resulted in better tablet hardness, dissolution profile, and disintegration time compared to single superdisintegrant. Similar results also reported from several studies (Kumar, 2012; Patil, 2011).

However, another study shown that type and proportion of fillers-binders used in a formula can affect the physical characteristics of tablets. Himabindu (2011), reported different physical tablet properties of Metoprolol Tartrate ODT was observed while different type filler-binders used in the ODT's formula. Result of these studies show that proportion of superdisintegrants and fillers-binders used in ODT formulation affect the physical

characteristics of tablets. Therefore, study should be generated to know the optimum proportion of filler-binder and superdisintegrant combination which results in best physical properties of ODT.

In this study, we optimize proportion of superdisintegrant combination of croscarmellose sodium and crospovidone and microcrystalline celullose as filler binder used in meloxicam-β-cyclodextrin ODT. Inclusion complex was done by spray drying techniques according to a previously published procedure from Purnamasari (2014). Effect of superdisintegrant combination and filler-binder were studied to obtain optimum formula of ODT which have good physical properties and dissolution profile.

2. METHODS OF PROPOSED SYSTEM

Meloxicam was purchased from Dongbang Future Tech & Life Co., Ltd. (Kyungki-do, South Korea). β-Cyclodextrin were obtained from Roquette Korea Ltd (Seoul, Korea Selatan). Ac-di-sol® dan Avicel® PH 200 were gifted from FMC Biopolymer (Philadelphia, USA). Kollidon-CL® were purchased from BASF chemical company. (Limburgerhof, Germany), Cab-o-sil® was purchased from Wecker Chemical South Asia (Singapore). PEG 6000 was purchased from Clariant (Germany) and Tropicana Slim® purchased from PT. Nutrifood (Indonesia). All other ingredients used were pharmaceutical grade.

Preparation of Meloxicam – β-Cyclodextrin Inclusion Complex: Meloxicam-β-cyclodextrin complex was prepared using the spray drying method according to a previously published procedure from Purnamasari (2014). β-cyclodextrin and meloxicam were weighed in 1:2 molar ratio. Then, β-cyclodextrin was dissolved in water with ratio of 1:30. Suspension of meloxicam - β-cyclodextrin was made by using methanol as a wetting agent for Meloxicam, and mixed with a solution of β-cyclodextrin to obtain a suspension of meloxicam-β-cyclodextrin. The suspension was dried using spray drier (Lab Plant SD-Basic). The inlet and outlet temperatures were 120^{o}C and 60^{o}C, respectively.

Preparation of tablets: Meloxicam ODT was produced with direct compression method according to a previously published procedure from Ghorab (2004). All ingredients were manually screened through 0.5-mm screen. An amount of the complex (Meloxicam-β-cyclodextrin) equivalent to 7.5 mg of meloxicam was blended with directly compressible filler-binder, microcrystalline celullose with cube mixer (Erweka AR-400) for 15 minutes. Crospovidone, croscarmellose, Cab-o-sil® were added, and the mixture was blended further for 10 minutes. Finally, 1% PEG 6000 as a lubricant was added and the mixture was blended for 5 minutes. The blend was then compressed using a single-punch tablet press (Korsch) using 9-mm diameter circular punch. Fifteen formulations were prepared with a target mass of 200 mg (formulas developed were shown in Table 1).

Pre-compression analysis: Powder blends were analyzed for pre-compression parameters, such as: Carr's compressibility index, Hausner ratio, and static angle of repose. Hausner ratio obtained by measured the ratio of tapped density to the bulk density. Carr's compresibility index was calculate using: C_I = ((tapped density – bulk density) / tapped density) x 100%. Angle of repose of the granules was evaluated by carefully poured through the funnel with closed bottom funnel. The height of conical pile formed and the radius of the base of the granules conical pile were also measured to acquire static angle of repose. Angle of repose was calculate using this equation: $\alpha = \tan^{-1}$ h (height of conical pile formed) / r (radius of the base of granules conical pile).

Characterization of meloxicam ODT: Weight variation were measured by randomly selected 20 tablets from each formula and individually weighed. The average weight of these selected tablets was calculated. Hardness of tablets was tested used Monsato Hardness Tester. Drug Content Uniformity was obtained by taking randomly ten tablets to the 100.0 ml volume flask. 5.0 mL of methanol and 1.0 mL NaOH 0.1 N were added into the flask then diluted by phosphate buffer pH 6.8 up to 100.0 ml. Drug content then analyzed by Spectrophotometry UV at 364 nm. Tablet friability was measured using a Rolling and Impact Durability Tester at 25 rpm for 4 min. The weight of twenty tablets before (Wo) and after (W) completion of the test was recorded and friability was calculated by the following formula: Friability (%) = (Wo-W)/Wo x 100%. Wetting time was tested by method developed by Singh and Singh (2008); Elbary (2012). Five circular tissue papers (10 cm diameter) to stimulate the tongue conditions were placed in a Petri dish with a 10 cm diameter. 10 ml of water containing Methylen blue 0.1% was added to the Petri dish. The tablet was carefully placed on the surface of the tissue paper. The time required for water to reach the upper surface of the tablets was noted as wetting time. *In vitro* disintegration time was tested by placing ODT in the petri dish (5 cm diameter). 20 ml of water was added to the petri dish. Disintegration time of six tablet were recorded.

***In vitro* dissolution study:** *In vitro* dissolution studies were carried out using USP type II apparatus at 50 rpm. Phosphate buffer (900 ml) at pH 6.80 (corresponding to salivary pH) was used as the dissolution medium. The temperature of the dissolution medium was maintained at 37±0.5^{0}C. 5 ml of aliquots were sampled in 1, 3, 5, and 10 minutes. Sink conditions were maintained by replenishing the medium with an equal amount (5 ml) of dissolution fluid. Absorption of the solution was measured by UV spectroscopy at 364 nm.

Optimization with Experimental Design: D-optimal design was employed using Design Expert Software (Version 7.1.5, Stat- Ease Inc, Minneapolis, MN) as per the standard protocol. The amount of Ac-di-sol® (A), Kollidon®-CL (B) and Avicel® PH 200 (C) were selected as the factors, studied at low and high levels each. All other formulation and processing variables were kept invariant throughout the study. Table 1 summarizes total 15 experimental runs and proportion of each factors studied. Hardness, friability, wetting time, disintegration time, uniformity content, and ammount of drug released (Q 3 min) were taken as the response variables.

3. RESULTS AND DISCUSSION

Powder blend were evaluated for it's flowability and compressibilty. The results were tabulated in Table 2. All formula were found to have good flowability as determined by Hausner's ratio, Carr's compressibility index and angle of repose. The compressibility index observed for all formulas were below to 19%. Compressibility index values of 12-16% generally indicate excellent flow properties in regard to compressibility-flowability correlation data. Hausner's ratio were found between 1.14-1.23, the angle of repose ranged from 19.92-24.44° for all the formulation blends. Therefore, the values of pre-compression parameters were within the prescribed limits and indicated excellent flow properties.

Result of physical properties and dissolution study of meloxicam ODT is presented in Table 3. Weight variation was found to be 198.05 – 201.65 mg. This result indicates that meloxicam ODT is meeting the requirements of weight uniformity (B.P, 2013). Thus indicating consistency in the preparation of the tablets and minimal batch to batch variation. The mechanical strength of pharmaceutical compacts is defined as the force required to fracture a specimen across its diameter, which is usually reported as tablet hardness (Martinello, 2006). The hardness test indicated good mechanical strength in all formulations. Hardness were found 3.26 - 3.63 kg/cm^3. The percentage friability was found to be 0.4 - 0.69%, which is below 1%, indicating that the friability is within the prescribed limits. Tablet hardness and friability of each formulas were not signifficantly different. Content uniformity of all formulas were also within the official requirements. Acceptance value of 15 formulas developed were between 5.51-11.74.

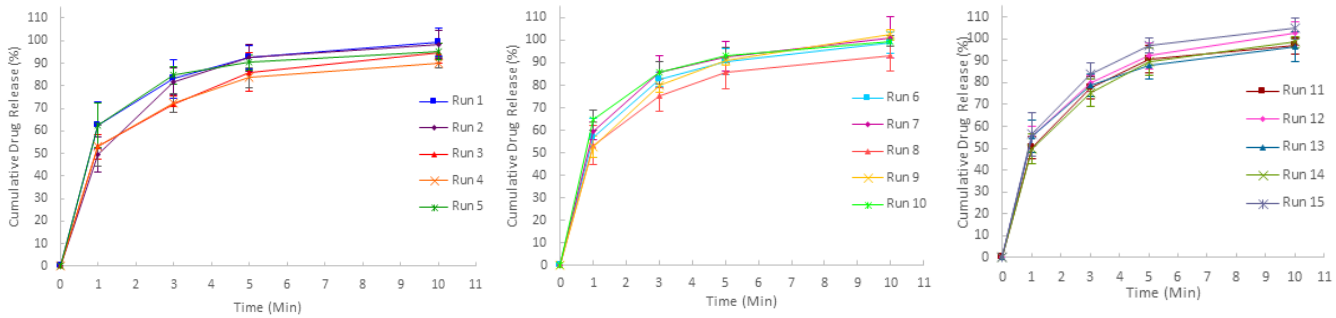
Wetting time of all formulas developed were found less than 19 sec. The shortest wetting time was obtained from Run 1 (contain 3.5 % croscarmellose sodium, 5 % crospovidone, and 51.5 % microcrystalline celullose). Another important parameter that needs to be optimized in the development of ODT is the disintegration time of tablets. In the present study, all the tablets disintegrated in 14 sec. The fastest disintegration time obtained on Run 5 (contain 2 % croscarmellose sodium, 5 % crospovidone, and 53.5 % microcrystalline celullose). Those results shown that minimum wetting time and disintegration time were obtained in formula contain high proportion of crospovidone and low proportion of croscarmellose sodium. This is allegedly due to high intraparticle porosity owned by microcrystalline celullose (Thoorens, 2014), which reduced swelling's capability, the main disintegration mechanism of croscarmellose sodium. For crospovidone, which mainly act by capillary action, maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particle (Nandi, 2011). Dissolution of meloxicam is presented as cumulative percent released over time. Dissolution testing in phosphate buffer pH 6.8 reveals that more than 70% of the drug gets released within 3 min for all the formulations with R7 showing maximum release of 85.95% (see Fig. 1).

Analysis of variance of the responses indicated that response models developed for disintegration time, wetting time, and cumulative drug release (%) were significant and adequate (p value model observed were <0.05). Influences of formulation variables on the response factors along with model summary statistics for the selected significant models are tabulated in Table 4. Wetting time's model equation shows that increasing concentration of croscarmellose sodium and crospovidone will greatly decrease wetting time, while increase microcrystalline celullose will slightly decrease the wetting time. However, effect of crospovidone seems to be more pronounced compared with croscarmellose sodium. Contour plot for wetting time are shown in Fig. 2. Based on those counterplots, we can argue that optimum concentration of croscarmellose sodium was observed at 3.5%. Addition of this concentration result in greatly increase of wetting time, while smaller concentration will slightly increase the wetting time. This pattern applies to all formulas developed except in Run 9.

Equation model of disintegration time shows that enhancement of croscarmellose sodium will increase disintegration time, while added of crospovidone result the opposite effect. Smaller croscarmellose sodium added, shortest disintegration time will be. Contour plot for wetting time are shown in Fig. 3. Disintegration action of croscarmellose sodium at low concentrations in tablet is due to its fibrous nature, which allows wicking of water into tablet matrices. At lower concentrations the fibrous nature is more pronounced and smoothens gradually with time. At high concentrations, there is a probability that wicking and swelling occurs simultaneously thus, smoothening the particles and the width of the pore decreases (Jagdale, 2010). High concentration of croscarmellose sodium also form viscous gel layer which can hindered penetration of disintegrate medium then prolonged tablet's disintegration (Rowe, 2009).

Tabulated D-optimal's equation of cumulative drug released (Q_{3min}) shows cumulative drug release can enhance by increase concentration of croscarmellose sodium, crospovidone, and microcrystalline celullose, eventhough crospovidone seems to be more pronounced compared with the other. Response surface plots shown in Fig. 4. Based on the counterplots, we know that the percentage of drug released were decreased as reduction of crospovidone used in formula. Decrease of croscarmellose sodium and microcrystalline celullose also affect in decrease of percentage of drug released. However, the alteration caused by these component not as great as caused by crospovidone. Crospovidone exhibits high capillary activity and pronounced hydration with a little tendency of gelling formation and disintegrate tablets into larger masses of agregat particles. On the other side, croscarmellose sodium will rapidly swelling and disintegrate tablet into apparently primary particles (Setty, 2008; Rao, 2009). However, high tablet porosity results in decrease swelling's capability.

Optimum formula were developed based on desired responses, then optimization technique using desirability approach was employed. Selection was based on the constraints set at appropriate limits and importance. Wetting time with a minimum target were set to ++++ importance, then minimum disintegration time and maximum ammount of drug release were set to +++++ importance. Tablet hardness, friability, and uniformity of content, which is non significantly different with each formulas developed were set as in range target. Desirability area were shown in Fig. 5. Optimum area were observed with in 2.00 - 4.11% croscarmellose sodium, 4.11 – 5.00% crospovidone, and microcrystalline celullose in 51.78 - 53.00%. Area with the highest desirability point were choosed as optimum formula. The optimum formula was obtained in 2.53% croscarmellose sodium, 5% crospovidone, and 52.47% microcrystalline celullose with the values of predicted response variables given by the software was found to be, 9.52 sec of disintegration time, 10.77 sec of wetting time, 83.82% of drug released in 3 min. Tablet hardness, and friability were found to be 3.42 kg/cm^3 and 0.53%, respectively. Verification was employed with one sample t-test between the predicted and the actual values. Statistic analysis shows that Sig. (2-tailed) off all parameter >0.05, so we can conclude that there is no significantly different between predicted and actual results, then all equation obtained can be used to compose formula which results in optimum physical characteristics of meloxicam ODT.



(A) **(B)** **(C)**

Figure.1.*In-vitro* dissolution profile of Run 1-5 (A), Run 6-10 (B), Run 11-15 (C) Meloxicam-β-cyclodextrin in phosphate buffer pH 6.8

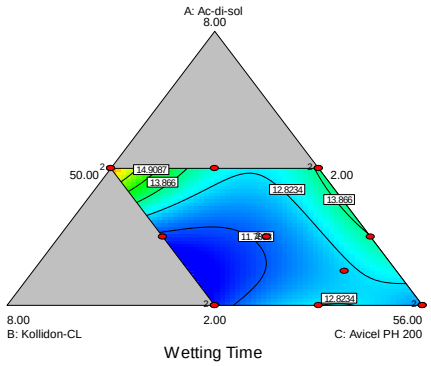


Figure.2.Contour plot of relationship between various levels of croscarmellose sodium, crospovidone, and microcrystalline cellulose on wetting time

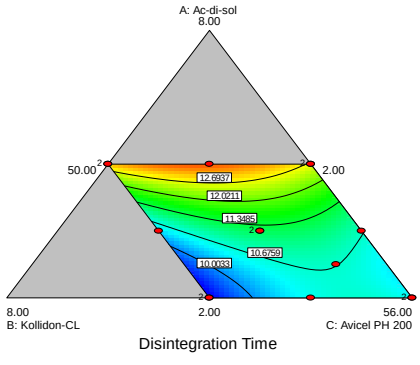


Figure.3.Contour plot of relationship between various levels of croscarmellose sodium, crospovidone, and microcrystalline cellulose on disintegration time

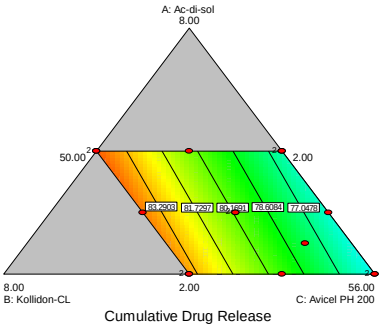


Figure.4. Contour plot of relationship between various levels of croscarmellose sodium, crospovidone, and microcrystalline cellulose

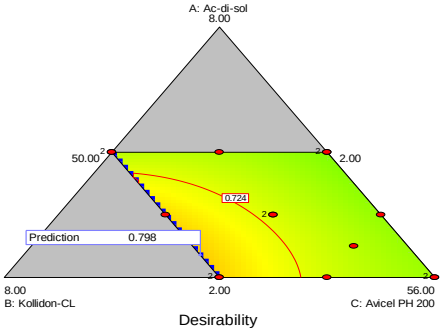


Figure.5. Desirability area of optimum formula of Meloxicam ODT

Table.1. Composition of Meloxicam-β-cyclodextrin ODT and proportion of each factors studied.

Formula	Ingredients (mg)								
	MLX-β-CD[a]	CCS	CP	MCC PH 200	Cab-o-sil®	PEG 6000	Tropicana ®	Aspartame	Total
R1	55,95	7	10	103	2	4	17,85	0,2	200 mg
R2	55,95	10	10	100	2	4	17,85	0,2	
R3	55,95	5,5	5,5	109	2	4	17,85	0,2	
R4	55,95	4	4	112	2	4	17,85	0,2	
R5	55,95	4	10	106	2	4	17,85	0,2	
R6	55,95	7	7	106	2	4	17,85	0,2	
R7	55,95	7	7	106	2	4	17,85	0,2	
R8	55,95	4	4	112	2	4	17,85	0,2	
R9	55,95	7	4	109	2	4	17,85	0,2	
R10	55,95	4	10	106	2	4	17,85	0,2	
R11	55,95	10	4	106	2	4	17,85	0,2	
R12	55,95	10	7	103	2	4	17,85	0,2	
R13	55,95	4	7	109	2	4	17,85	0,2	
R14	55,95	10	4	106	2	4	17,85	0,2	
R15	55,95	10	10	100	2	4	17,85	0,2	

Table.2. Pre-compression parameters of meloxicam-β-cyclodextrin ODT.

Run	Bulk Density* (g/cm^3)	Tapped Density* (g/cm^3)	Carr's Index (%)	Hausner's Ratio	Angle of Repose* (^{0})
R1	0.444 ± 0.003	0.523 ± 0.001	15.06 ± 0.82	1.18 ± 0.01	22.13 ± 0.57
R2	0.446 ± 0.002	0.536 ± 0.005	16.83 ± 0.82	1.20 ± 0.01	21.63 ± 0.75
R3	0.429 ± 0.003	0.499 ± 0.002	14.05 ± 0.33	1.16 ± 0.004	22.62 ± 0.28
R4	0.458 ± 0.003	0.508 ± 0.004	12.60 ± 0.8	1.14 ± 0.01	23.43 ± 0.56
R5	0.433 ± 0.004	0.520 ± 0.003	17.03 ± 0.32	1.20 ± 0.01	22.73 ± 0.09
R6	0.434 ± 0.002	0.534 ± 0.003	18.79 ± 0.66	1.23 ± 0.01	23.14 ± 0.57
R7	0.433 ± 0.004	0.531 ± 0.005	18.51 ± 0.37	1.23 ± 0.01	21.31 ± 0.5
R8	0.441 ± 0.003	0.497 ± 0.002	13.48 ± 1.02	1.16 ± 0.01	23.43 ± 0.28
R9	0.447 ± 0.002	0.523 ± 0.003	14.64 ± 0.4	1.17 ± 0.01	24.44 ± 1.96
R10	0.431 ± 0.002	0.522 ± 0.005	17.46 ± 0.46	1.21 ± 0.01	22.73 ± 0.09
R11	0.434 ± 0.002	0.508 ± 0.001	14.94 ± 0.39	1.18 ± 0.01	22.62 ± 0.28
R12	0.440 ± 0.003	0.524 ± 0.002	15.93 ± 0.28	1.19 ± 0.004	19.92 ± 0.21
R13	0.436 ± 0.002	0.522 ± 0.005	16.47 ± 0.46	1.20 ± 0.01	23.14 ± 0.57
R14	0.431 ± 0.002	0.51 ± 0.003	15.83 ± 0.66	1.19 ± 0.01	22.31 ± 0.81
R15	0.448 ± 0.007	0.537 ± 0.003	16.66 ± 0.89	1.20 ± 0.01	22.92 ± 0.66

Table.3. Post-compression parameters of meloxicam-β-cyclodextrin ODT.

Run	Parameters						
	Weigh Unifromity (mg)	Hardness (Kg/cm3)	Friability (%)	Wetting Time (sec)	Disintegration Time (sec)	Content Unifromity (AC)	Q 3min (%)
R1	198.75 ± 2.99	3.45 ± 0.25	0.55 ± 0.04	11.13 ± 0.6	10.25 ± 0.76	10.14 ± 1.52	83.06 ± 8.46
R2	199.45 ± 1.83	3.44 ± 0.29	0.64 ± 0.01	16.63 ± 0.89	13.80 ± 0.59	7.18 ± 1.31	81.8 ± 5.85
R3	199.45 ± 1.80	3.63 ± 0.19	0.41 ± 0.09	12.04 ± 0.44	10.62 ± 1.57	9.99 ± 2.52	71.98 ± 3.61
R4	201.65 ± 2.41	3.41 ± 0.2	0.47 ± 0.05	11.94 ± 0.95	10.72 ± 0.84	7.27 ± 1.36	72.30 ± 4.16
R5	198.05 ± 1.66	3.47 ± 0.23	0.64 ± 0.08	11.51 ± 1.05	9.33 ± 0.44	5.51 ± 1.31	84.54 ± 3.88
R6	198.7 ± 1.45	3.49 ± 0.22	0.4 ± 0.04	12.16 ± 1.12	11.19 ± 0.87	9.19 ± 2.23	82.66 ± 1.42
R7	198.55 ± 2.46	3.39 ± 0.31	0.49 ± 0.11	11.64 ± 0.97	11.59 ± 0.48	10.60 ± 2.88	85.95 ± 6.96
R8	198.9 ± 1.61	3.37 ± 0.17	0.56 ± 0.05	12.27 ± 1.29	10.36 ± 0.72	11.57 ± 2.46	75.33 ± 7.11
R9	200.05 ± 2.22	3.47 ± 0.18	0.49 ± 0.03	14.83 ± 0.95	10.53 ± 0.78	9.80 ± 1.78	80.14 ± 3.15
R10	199.5 ± 1.99	3.26 ± 0.16	0.56 ± 0.1	11.67 ± 0.64	9.49 ± 0.23	8.99 ± 2.24	85.61 ± 5.11
R11	200.55 ± 2.11	3.58 ± 0.18	0.69 ± 0.08	14.31 ± 0.99	12.39 ± 0.6	10.09 ± 1.63	77.72 ± 5.21
R12	200.2 ± 1.94	3.42 ± 0.31	0.57 ± 0.04	13.97 ± 0.66	13.52 ± 0.88	7.04 ± 1.93	79.75 ± 3.80
R13	199.5 ± 1.66	3.50 ± 0.28	0.58 ± 0.12	12.62 ± 0.81	10.20 ± 0.73	9.93 ± 2.51	78.61 ± 5.02
R14	199.55 ± 2.66	3.41 ± 0.27	0.59 ± 0.03	12.93 ± 0.57	12.85 ± 0.81	11.27 ± 2.08	75.32 ± 6.05
R15	199.45 ± 2.20	3.51 ± 0.2	0.4 ± 0.04	18.46 ± 0.95	12.33 ± 0.75	11.74 ± 1.60	83.73 ± 5.53

Table.4. Statistics summary and D-optimal equation for the selected significant models

Responses Factor	Actual D-Optimal Equation	Model		Lack of fit
		F value	Prob > F	
Hardness	Y = 0.075(A) + 0.044(B) + 0.057(C)	0.67	0.5322	0.6004
Friabiity	Y = 2.39(A) + 0.255(B) + 0.012(C) - 0.067(AB) - 0.043(AC) - 0.003(BC)	1.70	0.2305	0.7209
Uniformity of content	Y = - 0.139(A) – 0.351(B) + 0.191(C)	4.72	0.3303	0.5788
Wetting time	Y = -70.1(A) - 79.3(B) - 0.28(C) + 28.53 (AB) + 1.43(AC) + 1.57(BC) - 0.54(ABC)	13.57	0.008	0.3102
Disintegration time	Y = 19.8(A) - 15.9(B) + 0.185(C) + 0.102(AB) - 0.362(AC) + 0.291(BC)	28.98	<0.001	0.8952
Dissolution	Y = 1.48(A) + 3.88(B) + 1.16(C)	0.0049	8.58	0.0484

4. CONCLUSION

From the present study, it may be concluded that desirability or optimum area were observed with in 2.00 - 4.11% croscarmellose sodium, 4.11 – 5.00% crospovidone, and microcrystalline cellulose in 51.78 - 53.00%. Optimum physical tablet properties of meloxicam-β-cyclodextrin ODT obtained with proportion of 2.53% croscarmellose sodium and 5% crospovidone, and 52.47% microcrystalline cellulose. Overall, crospovidone seems to be more pronounced compared with other component in order to obtain optimum formula of meloxicam β-cyclodextrin ODT.

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