The Influence of Avicel PH 102 as Filler-Binder Agent and Explotab as Disintegrant Agent Against Andrographolide Dissolution Rate Of Sambiloto Extract Tablets

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Abstract

*Sambiloto (*Andrographis paniculata *Ness) is one of the constituent materials traditional medicine concoction as anti-diabetes on the various dosage forms, such as powder, capsule, and tablet. Avicel is one of the pharmaceutical filler-binder agents on the direct compression tablet. Explotab is disintegrator agent in tablet formulation, by either direct compression or wet granulation process. The aim of this research is to find out the influence of Avicel PH 102 and Explotab againts andrographolide dissolution rate of sambiloto extract tablets. The tablets were made by direct compression with factorial design 2^2 using 20% and 90% Avicel PH 102 and 2% and 8% EXPLOTAB, of extracts weight, respectively, were independent variables. The dissolution andrographolide response as dependent variables. The experiment was conduct in the formulation technology laboratory, Universitas Gadjah Mada, Yogyakarta. Based on dissolution rate data, the formulation are expressed in the factorial experimental design: Y = 34.52 + 33.37Xa + 12.54Xb + 11.39XaXb, which figured out the influence of Avicel PH 102 (Xa), Explotab (Xb) and their interaction (XaXb). The Avicel PH 102, Explotab, and their interaction significantly increase the andrographolide dissolution rate of the sambiloto's extract tablet, while Avicel PH 102 dominantly increase the dissolution rate (Q_{45}) of andrographolide.*

Key words: *Avicel PH 102, Explotab and dissolution andrographolide.*

INTRODUCTION

Dissolution tests have been widely used in pharmaceutical industry to characterize the release of drug from dosage forms. It is needed in many stages in drug development life cycle. Dissolution was introduced more than 30 years as the quality control tools to assure product uniformity and detect batch-to-batch differences of drug products occurring during the manufacture processes(Leeson, 2973). Dissolution tests are simple, reliable, highly reproducible methods that allow monitoring the product quality efficiently and could be used to establish the equivalence between formulations at different stage of development (Tong et al., 2007).

Sambiloto (*Andrographis paniculata* Ness) is one of the constituent materials of the traditional medicine concoction as anti-diabetes which applied with other plants on the various dosage forms, such as pulv, pillulae, capsule, and caplete (Anonim, 2008). Andrographolide is medicinally the most active phytochemical in *A. paniculata* (Vijaykumar *et al*., 2007; Raina *et al*., 2007) and has been used to treat diabetes mellitus (Subramanian *et al*., 2008).

The tablet preparation of aqueous extract of *A.paniculata* aerial parts have been conducted by Mshelbawala (2007), with maize starch as disintegrator agent

and lactose as diluents which produce a hygroscopic granule having high moisture content ranging from 24-36% (Mshelbwala, et al., 2007). The hygroscopic material could not be processed by wet granulation because it became very sticky when exposed to water. To avoid a solvent granulation process, a formulation for direct compression was developed (Labella, 2005). Tablet made by direct compression should be disintegrated rapidly to the primary particle state; it can certainly speed up the dissolution process (Shangraw, 1989).

One of the pharmaceutical filler-binder on direct compression is cellulose microcrystalline (Avicel). It works as an adsorbent (Rowe, et al., 2009) and it can adsorb the small quantity of water on the granule (Shangraw, 1989). It has been found that formulations containing more than 80% Avicel may slow the dissolution rates of active ingredient having low solubility (Shangraw, 1989). Generally, tablets will be disintegrated before it is disoluted. Sodium Starch glycolat (Explotab) is one of the disintegrator agent of the direct compression tablet (Rowe, et al., 2009), it has strongly swelling carriers (Bolhuis, et al., 1997). On a high concentration, however, Explotab acts as a binder agent due to the forming of viscous barrier and it is causing the excalation of tablet disintegration time (Bolhuis, et al., 1997). The aims of this research is to find out the influence of Avicel PH 102 and Explotab against the dissolution rate (Q_{45}) of sambiloto's extract tablet.

MATERIALS AND METHODS

Sambiloto was obtained from medicinal plant garden Matesih, Karanganyar regency-Central Java. Avicel PH 102 (Comprecel, type M102D+), Explotab (Sodium Starch Glycollate-Gujarat Overseas), Andrographolid Sigma, Plat KLT-KT Silicagel GF_{254} (E.Merck), Ethanol 90% and hexane were used.

The tablets were made by direct compression using Avicel PH 102 and explotab. A 2^2 factorial design was used to investigate the amount of Avicel PH 102 and explotab as independent variables. The andrographolide dissolution of sambiloto extract tablets were dependent variables.

The preparation of sambiloto extract was made by maceration powder herbs with ethanol 90%. The extract was concentrated on a rotary evaporator and evaporated to a certain thickness. The viscous extract was purified by washing the extract with hexane. The purified extract was further dried in a hot air oven at 40^0C which brought it to complete dryness. The dry extract was sized reduced using grinding machine and sieved through 50 mesh sieve. Each tablet contained 80 mg of dry extract, and the other exipients weighed based on the extract weight. The composition of Avicel PH 102 and explotab in the sambiloto extract tablet is shown on table 1.

Table 1. Factorial design 2^2 used to produce sambiloto extract tablet

Formula	Extract (mg)	Avicel PH 102 (%)	Explotab (%)
(-1)	80	20	2
a	80	90	2
b	80	20	8
ab	80	90	8

Remark:
(-1) mixing of Avicel PH 102 low level with Explotab low level
a mixing of Avicel PH 102 high level with Explotab low level
b mixing of Avicel PH 102 low level with Explotab high level
ab mixing of Avicel PH 102 high level with Explotab high level
% of Avicel PH 102 and EXPLOTAB based on extracts weight (80 mg) respectively

The dissolution studies were carried out using the paddle method (apparatus II), the rotational speed of the paddle was set at 50 rpm, taking 900 ml of buffer acetat pH 4,5 dissolution medium with 9 ml Sodium Lauryl Sulphate 0,1 M, at 37 ± $0,5^0$C. The aliquot withdrawn at minutes-45.

The determination of andrographolide content used The HPTLC method. The chromatography was performed on Silicagel GF254 HPTLC plates with TLC applicator Linomat-5. The mobile phase was $CHCl_3$:MeOH (9:1).

RESULTS AND DISCUSSION

The tablet hardness is controlled constantly and the result achieved is between 4.2-5.43 kg. The tablet hardness may influence the tablet disintegration and perhaps more significantly, drug dissolution release rate have become apparent (Fonner, et al., 1981). In this research, the tablet hardness is controlled constantly so that dissolutin rate can only be influenced by the tablet formula. It means that the dissolution rate was influenced by the number of Avicel PH 102 and Explotab, respectively.

The result of determination Physical properties of tablet sambiloto extract exhibited on table 2.

The result of andrographlide dissolution rate of sambiloto extract tablet on 45 minute stated on table 3.

The influence of each component with their interaction versus the dissolution release time has been known from the value of equation coefficient. Based on the coefficient value, Avicel PH 102 (+33.37) has greater influence than Explotab (+12.54) to the dissolution rate. Probably, it happens because the primary particle of Avicel PH 102 are composed of microfibrils with high porosity (Bolhuis & Chowhan, 1996 in Aldenborn & Nystrom, 1996).

Table 2. The Result of Determination Physical Properties of Tablet sambiloto Extract

Parameter	(-1)	a	b	ab	Literature
Tablet hardness (kg)	5.37 ± 0.01	4.27 ± 0.02	5.43 ± 0.04	4.2 ± 0.00	4-8 kg (Parrott, 1971)
Andrographolide content of the tablet	91.41 ± 0.07	92.51 ± 0.30	91.71 ± 0.1	92.35 ± 0.2	85-115 % (Anonim, 1995[a])
Uniformity of andrographolide content	91.71 ± 0.3 KV = 2.65%	92.81±0.16 KV = 1.73%	90.44±0.61 KV = 2.70%	91.45±0.47 KV = 2.14%	85-115% (Anonim, 1995[a])

Table 3. Andrographolide dissolution rate of sambiloto estract tablets on 45 minute

	Batch 1				Batch 2			
Replicate	(-1)	(a)	(b)	(ab)	(-1)	(a)	(b)	(ab)
1	0	44,25	2,27	90,66	0	44,37	2,25	92,59
2	0	44,86	2,38	91,14	0	42,74	2,22	90,98
3	0	44,83	2,27	93,61	0	43,19	2,32	93,58
4	0	44,69	2,35	90,26	0	42,86	2,30	92,74
5	0	44,85	2,30	90,74	0	42,81	2,32	92,28
6	0	44,54	2,33	91,45	0	43,66	2,31	92,72
Average	0	44,67	2,32	91,31	0	43,27	2,29	92,28
SD	0	0,24	0,04	1,20	0	0,63	0,04	0,89
CV		0,53	1,88	1,31		1,47	1,90	0,97

Based on dissolution rate data, the formulation are expressed in the factorial experimental design:

$$Y = 34.52 + 33.37Xa + 12.54Xb + 11.39XaXb$$

(Xa) = Avicel PH 102

(Xb) = Explotab

Mostly, water will be inside the porous structure of Avicel PH 102 and disrupt the hydrogen bonds which connecting its molecule. This action is breaking up the tablet (Peck, et al., 1989). Later, Explotab will swell when contact with water to initiate the tablet disintegration. The tablet disintegrates into granul, and these granules deaggregate into fine particles (Martin, 1990). Explotab has less influence than Avicel PH 102 toward dissolution rate of the tablet. On the higher concentration, Explotab may act as a binder instead of swelling which causes gelling. Thus causing a viscous barrier (Bolhuis, 1997) and prevent diffusion of water within tablet and slow down the release of active compound to the medium. The contour plot of dissolution rate (Figure 1) showed the proportion of Avicel PH 102 is on the X bar and the proportion of Explotab is on the Y bar.

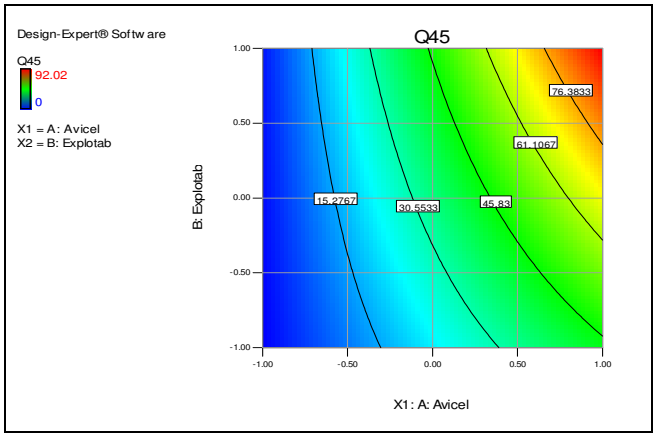

Figure 1. Contour plot of andrographolide dissolution rate of sambiloto extract tablet

The relative influence of Avicel PH 102 and Explotab concentration on the dissolution rate are demonstrated by the orange color of the graph which means the greater concentration of Avicel PH 102 & Explotab will increase the dissolution rate. The color which is degradated into blue means the less concentration of Avicel PH 102 & Explotab will decrease the dissolution rate.

CONCLUSION

Avicel PH 102, Explotab, and their interaction significantly increase the andrographolide dissolution rate of the sambiloto's extract tablet, while Avicel PH 102 dominantly increase the dissolution rate (Q_{45}) of andrographolide.

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