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THE OPTIMIZATION OF AVICEL PH 101 AND MANNITOL IN *Nigella sativa* L. EXTRACT TROCHES BY SIMPLEX LATTICE DESIGN

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ABSTRACT

Nigella sativa L. is one of herbs that can be used as antibacterial against *Streptococcus pyogenes*. We did the optimization of the avicel PH 101 and mannitol in *Nigella sativa* L. troches by simplex lattice design (SLD). The result showed that the optimum proportion formula was 0.1 part of avicel PH 101: 0.9 part of mannitol, with flow rate 11.5034 g/sec, moisture content 2.83%, compressibility 6.34%, hardness 4.26 kg, and friability 0.45%. The granule flow rate, moisture content, compressibility, hardness of troches with avicel PH 101 were bigger than troches with mannitol. The troches with avicel PH 101 had friability of troches smaller than the troches with mannitol, while the interaction of both ingredients had the biggest hardness of troches.

Key words: *Nigella sativa*, troches, optimization, simplex lattice design

INTRODUCTION

The seeds of *Nigella sativa*, which is under a botanical family of Ranunculaceae, has been claimed to have several traditional medicinal properties (Roshan, *et.al.*, 2010). The seed extracts and its essential oil have been reported to exhibit many pharmacological effects such as antioxidant (Yoruk, *et.al.*, 2010), antihepatocarcinogenic (Samarakoon, *et.al.*, 2012) and antibacterial (Zuridah, *et.al.*, 2008). As an antibacterial, *Nigella sativa* can become an alternative for curing sore throat, while *Streptococcus pyogenes* is one of bacteria can caused it.

Ethyl acetate and ethanolic extract of *Nigella sativa* seed which contain are flavonoid and saponin can inhibit *Streptococcus pyogenes* growth (Wulansari, *et.al.*, 2011). The *Nigella sativa* ethanolic extract formed into lozenges, gives good physical characteristic and preference taste (Wulansari, *et.al.*, 2012). Avicel PH 101 and mannitol are ingredients that usually used for making troches. Both ingredients influence to the physical characteristic of the result troches, so it has to optimize. One of the optimizing methods is *Simplex Lattice Design*. This method can be used for optimizing formula with different amount of many ingredients composition (Murrukmihadi, *et.al.*, 2011). The aim of this study is to find out the optimal proportion formula of *Nigella sativa* extract troches with avicel PH 101 and mannitol as ingredients.

MATERIAL AND METHODS

Material

The *Nigella sativa* seeds were purchased from a local herbal shop in Semarang, Indonesia. The other material are ethanol, avicel PH 101, mannitol, menthol, PVP K-30, coloring agent, and magnesium stearate.

Extraction procedure

A modified extraction method by Zaman, *et.al.* (2004) and Keyhanmanesh, *et.al.* (2007) was used. About 1 kg *Nigella sativa* seeds powder were macerated with 2 L of ethanol for 48 hours. *Nigella sativa* crude extract was evaporated using vacuum rotary evaporator.

Formulation of troches

The troches was formulated by using 10 % *Nigella sativa* extract, that its concentration can used as antibacterial against *Streptococcus pyogenes* growth. *Nigella sativa* extract were found to be safe up to 800 mg/kg per oral (Roshan, *et.al.*, 2010). Hence the concentration 10 % extract was selected for the formula. Formulation of *Nigella sativa* troches was using a formula:

Dried extract	10%
PVP	20%
Magnesium stearate	0.4%
Menthol	qs
Coloring agent	qs
Filler	till 500 mg

There were 3 formula, which formula A (100 % of avicel PH 101 as filler of troches), formula B (100% of mannitol as filler of troches), and

formula C (50% of avicel PH 101 and 50% of mannitol as filler of troches).

The troches were made by wet granulation method.

Physical characteristic test

The granules were tested by flow rate test, moisture content test, and compressibility test. All data from the test were used as granule optimum responsibility. The troches were tested by weight uniformity test, friability test, hardness test, and taste perception test. Data of friability and hardness test were used as troches optimum responsesibility.

Weight uniformity test : at amount of 20 troches were taken out randomly, and each troches weight was measured. The average weight of troches was calculated.

Friability test : at amount of 20 troches taken out randomly, weighted, cleaned up of dust and put it on the friability tester (Roche-Erweka). After running for 4 minutes (speed 25 rpm), the troches were cleaned and weighted.

Hardness test : at amount of 20 troches were taken out randomly and its hardness were measured with hardness tester (Stokes Mosanto-Prima).

Taste perception test : 30 troches for each formula were gift to 30 volunteers. The volunteers were asked to give their valuation about the taste of troches as sweetness, bitterness and pungent taste. The valuations were scored and calculate the most preferred taste troches.

RESULT AND DISSCUSSION

Fillers are important to decide the troches physical characteristic, so that in this research we did the optimizing of filler in the *Nigella sativa* extract troches in away to get good troches with the right filler composition. The physical characteristic of *Nigella sativa* extract of granule and troches with SLD equation are shown in the Table 1. The granule flow rate of formula B is the latest. Mannitol has large surface area and fines form, thus the cohesive force between the particles causes the particles agglomerate easily, the flow rate becoming poor. The good free flowing rate is more than 10g/sec (Sulaiman, 2007). Based on the SLD equation, avicel PH 101 has a greater influence than mannitol. So that flowing rate of granule with avicel PH 101 as filler are bigger than granule with mannitol as filler.

Moisture content of granule with the SLD equation showed that formula A had the highest moisture content. A high concentration of avicel PH 101 can cause moisture, even hygroscopes (Siregar, 2010). Based on SLD equation, decreasing of avicel PH 101 concentration in the mixture will decrease the moisture granule responses.

All filler, avicel PH101 or mannitol, can interfere the compressibility of troches. Avicel PH 101 can increase the compressibility, better than mannitol. The interaction between both substance can also cause the increasing of compressibility. Avicel PH 101 can fix the compressibility of

all troches. The good compressibility of granule is 5-15% (Sulaiman, 2007).

Hardness of troches is a parameter that describes the ability of troches to mechanical pressure while packaging to the consumer. The good hardness of troches is 7-14kg (Cooper and Gunn, 1975). All formula have hardness less than 7kg, it also because of the concentration of the binder. In this research, the extract was consisted of oily substance made poor hardness of troches. Based on SLD equation, avicel PH 101 has higher influence to the hardness of troches than mannitol.

A good friability of tablet is not more than 1 % (Sulaiman, 2007). Based on SLD equation, mannitol has bigger influences to the friability of troches.

Optimum formula granule extract of *Nigella sativa* can be determined by using parameter optimum response granule and troches, and by looking at the total values of highest response, as shown in Table 2. The optimum proportion formula was 0.1 part of avicel PH 101: 0.9 part of mannitol, are shown at Figure 1.

The comparison formula was used to verify it's SLD equation. This formula used the proportion avicel PH 101 0.2: mannitol 0.8. And the result showed that the SLD equation was valid. It showed that the granule flow rate of the optimum formula was 11.5034 g/sec, granule moisture content was 2.83%, compressibility was 6.34%, hardness of troches was 4.26 kg, and friability of troches was 0.45%. The granule flow rate, moisture

content, compressibility, hardness of troches with avicel PH 101 were bigger than troches with mannitol. The troches with avicel PH 101 had friability of troches smaller than the troches with mannitol. While the interaction of both ingredients had the biggest hardness of troches. The result of taste preference test was that the optimum formula taste sweeter and more pungent than the comparison formula. There was 87% respondent preferred the optimum formula.

CONCLUSION

In this study we have found that the optimum formula of *Nigella sativa* extract troches has good physical characteristics and can be accepted by the respondent. However, to make sure the stability of the troches, further studies will be required, especially regarding the troches of *Nigella sativa* which extract contain a lot of oily substance.

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Table 1. The physical characteristic of *Nigella sativa* extract granule and troches

Testing of	Formula A	Formula B	Formula C	SLD equation
Flow rate (g/sec)	15.4330 ± 0.1073	10.5487 ± 0.0501	14.2860 ± 0	Y= 15.433(A) + 10.5487(B) + 5.1804(A)(B)
Moisture content (%)	3.58 ± 0.0447	2.80 ± 0	3.06 ± 0.0894	Y= 3.58(A) + 2.8(B) – 0.52(A)(B)
Compressibility (%)	10.8 ± 0.4472	5.0 ± 0	10.0 ± 0	Y= 10.8(A) + 5(B) + 8.4(A)(B)
Hardness (kg)	4.35 ± 0.2415	4.00 ± 0	4.80 ± 0.2582	Y = 4.35(A) + 4(B) + 2.5(A)(B)
Friability (%)	0.1808 ± 0.0352	0.5188 ± 0.0447	0.2482 ± 0.0332	Y = 0.1808(A) + 0.5188(B) – 0.4064(A)(B)

Table 2. Determination of the optimum formula

A	B	R' 1	R' 2	R' 3	R' 4	R' 5	R total
1	0	0.0189	0.0947	0.0473	0.13	0.0819	0.3728
0.9	0.1	0.0196	0.1029	0.0515	0.092	0.0822	0.3482
0.8	0.2	0.0238	0.1106	0.0553	0.064	0.0817	0.3354
0.7	0.3	0.0315	0.1175	0.0588	0.046	0.0803	0.3341
0.6	0.4	0.0426	0.1238	0.0619	0.038	0.0782	0.3445
0.5	0.5	0.0571	0.1293	0.0647	0.04	0.0752	0.3663
0.4	0.6	0.0751	0.1342	0.0671	0.052	0.0714	0.3998
0.3	0.7	0.0966	0.1383	0.0692	0.074	0.0668	0.4449
0.2	0.8	0.6076	0.1418	0.0709	0.106	0.0614	0.9877
0.1	0.9	0.7494	0.1446	0.0723	0.148	0.0552	1.1695
0	1	0.1817	0.1467	0.0733	0.2	0.0481	0.6498
weight		0.2	0.2	0.1	0.4	0.1	

Note:

A (Avicel PH 101)

B (Mannitol)

R' 1 (Transformation response of granule flow rate)

R' 2 (Transformation response of granule moisture content)

R' 3 (Transformation response of granule compressibility)

R' 4 (Transformation response of hardness of troches)

R' 5 (Transformation response of friability of troches)

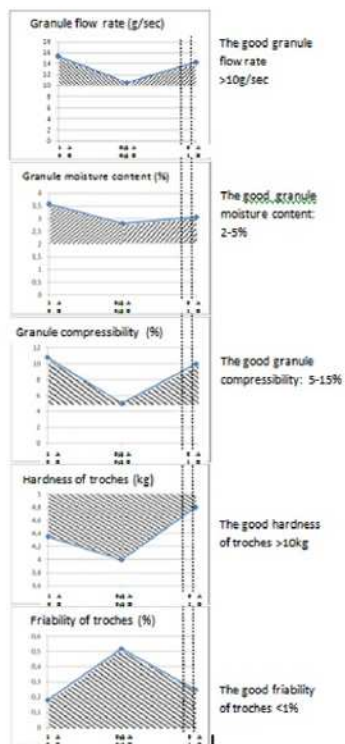


Figure 1. Profile of Optimum Area

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