



APPLICATION OF THE SIMPLEX LATTICE DESIGN METHOD IN OPTIMIZING THE FORMULA OF KOPASANDA LEAF EXTRACT CHEWABLE TABLETS



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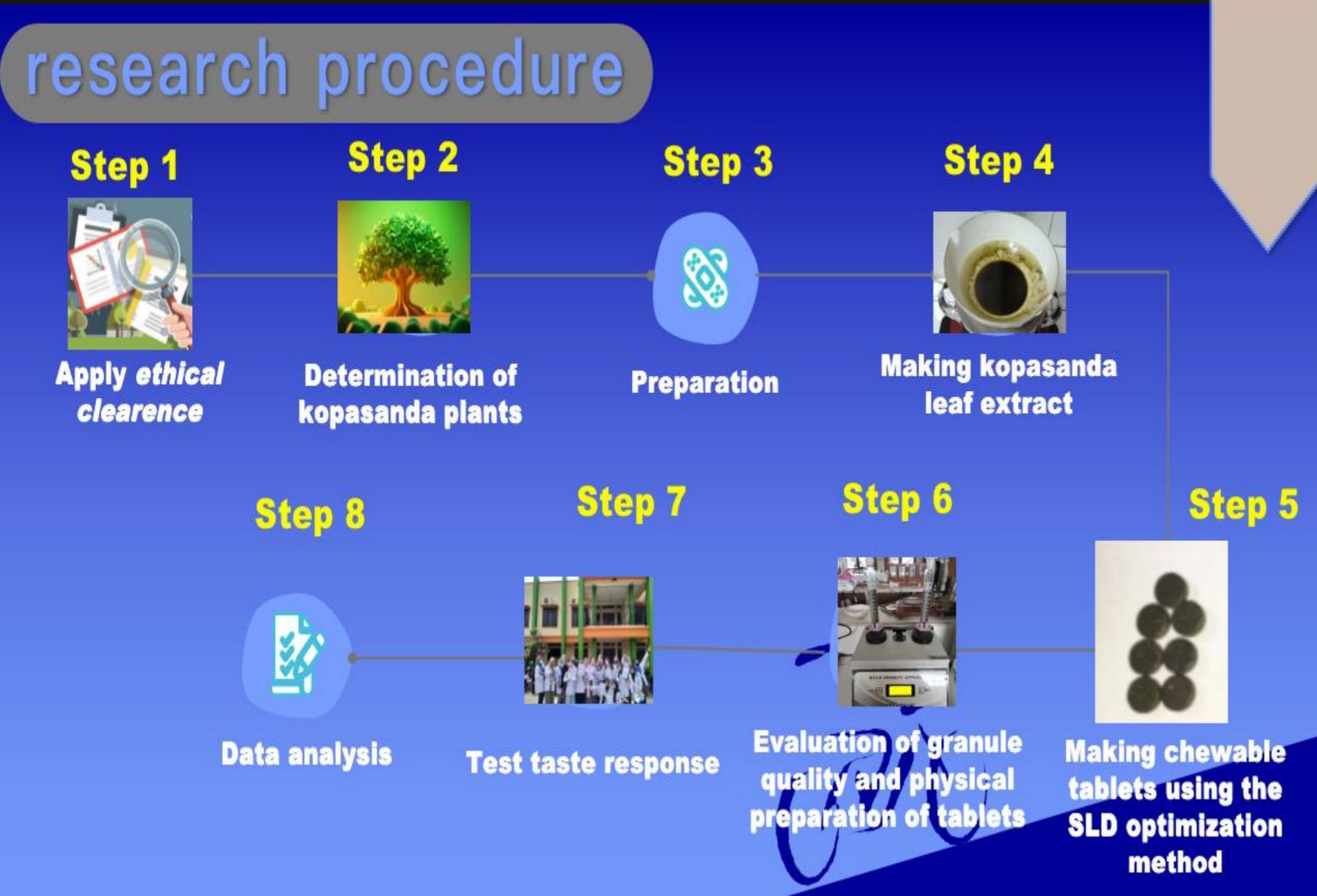
Background

Kopasanda plant (*Chromolaena odorata* L.) is a plant that lives in tropical and sub-tropical areas. The flavonoid content in kopasanda plants functions as an antioxidant, counteracts free radicals and as antihypercholesterolemia. According to research by Koban (2019), it shows that the ethanol extract of kopasanda leaves (*Chromolaena odorata* L.) at doses of 20 mg/kgBW, 40 mg/kgBW, and 60 mg/kgBW has antihypercholesterolemia activity in white rats induced by high fat. Kopasanda leaf extract at a dose of 60 mg/kgBW showed good antihypercholesterolemic effects (Koban et al., 2019). The use of kopasanda leaves (*Chromolaena odorata* L.) as a medicinal preparation is still limited. The dosage form of the kopasanda leaf plant for treatment is most widely circulated and most people consume it in the form of brewed tea, so it is necessary to develop a dosage form of kopasanda leaf extract into a suitable, practical and efficient dosage form. One of them is by making it into a chewable tablet dosage form, where the dosage form has several advantages, such as easy to consume, practical, the dosage is right, can be packaged well, practical, stability is maintained in storage (Putri, 2020). In formulating preparations, optimization methods are needed. This research optimized the formula for kopasanda leaf extract chewable tablets (*Chromolaena odorata* L.) by mixing the fillers mannitol and lactose to obtain the optimum proportion of both using SLD method. The Simplex Lattice Design (SLD) method only requires data from several experiments to obtain a profile of the physical properties of granules at various proportions of mannitol and lactose fillers.

Objectives

This research aims to determine the manufacture of chewable tablet formulas with variations of mannitol and lactose using the SLD optimization method, to find out the effect of the combined ratio of mannitol and lactose fillers on the physical properties of chewable tablets including hardness, brittleness, weight uniformity and disintegration time of chewable tablets, to find out at what concentration the combination of mannitol and lactose can produce optimum chewable tablets using the Simplex Lattice Design method. and to determine the qualitative stability of the flavonoid content in kopasanda leaf extract (*Chromolaena odorata* L.)

Methods



RESULT AND DISCUSSION

Based on the research results, 1500 grams of dry simplicia powder, 208.3 grams of thick extract was obtained with an extract yield of 13.886%. Based on the book Indonesian Herbal Pharmacopoeia (2017), it is stated that the thick extract of kopasanda leaves contains a total flavonoid content of not less than 3.84% with an extract yield of not less than 12.0% (Ministry of Health of the Republic of Indonesia, 2017). The yield of the extract obtained is 13.886%.

RESULT AND DISCUSSION

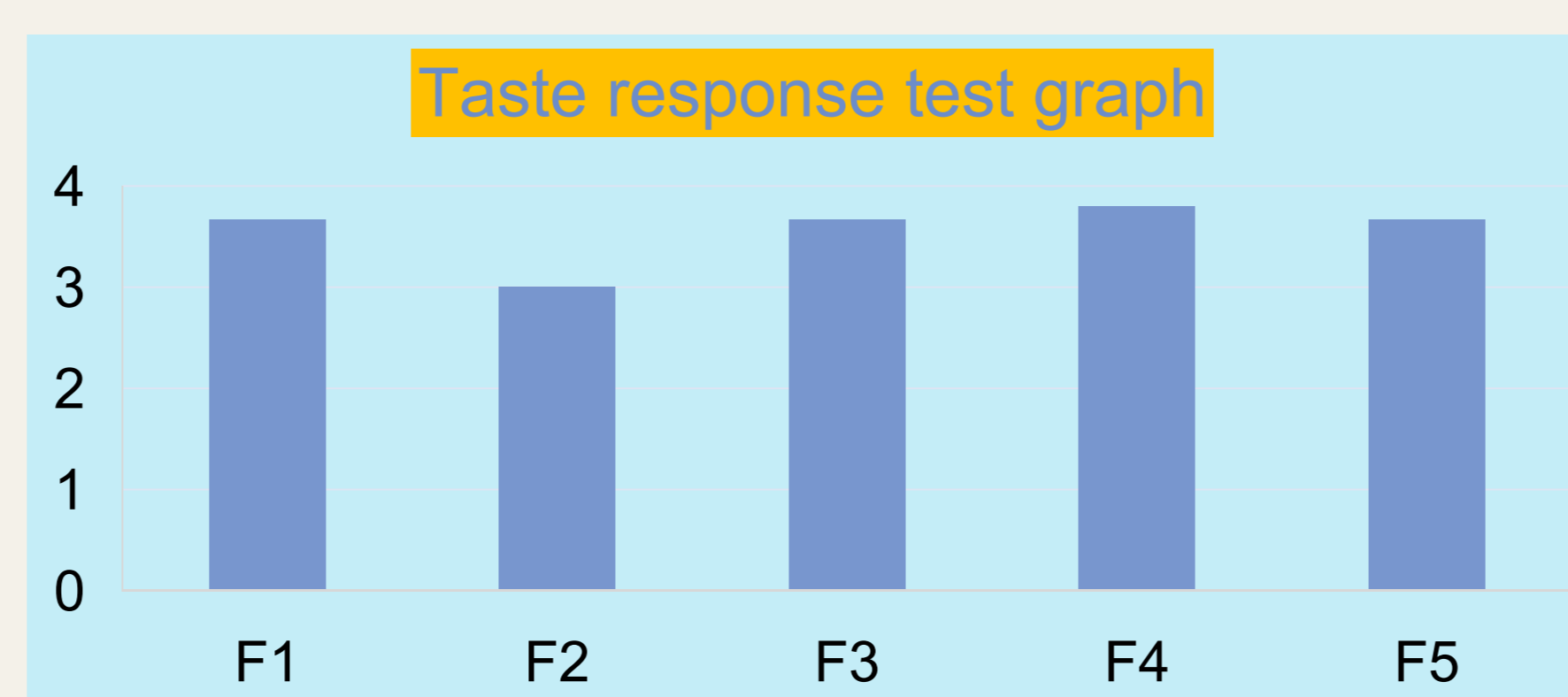
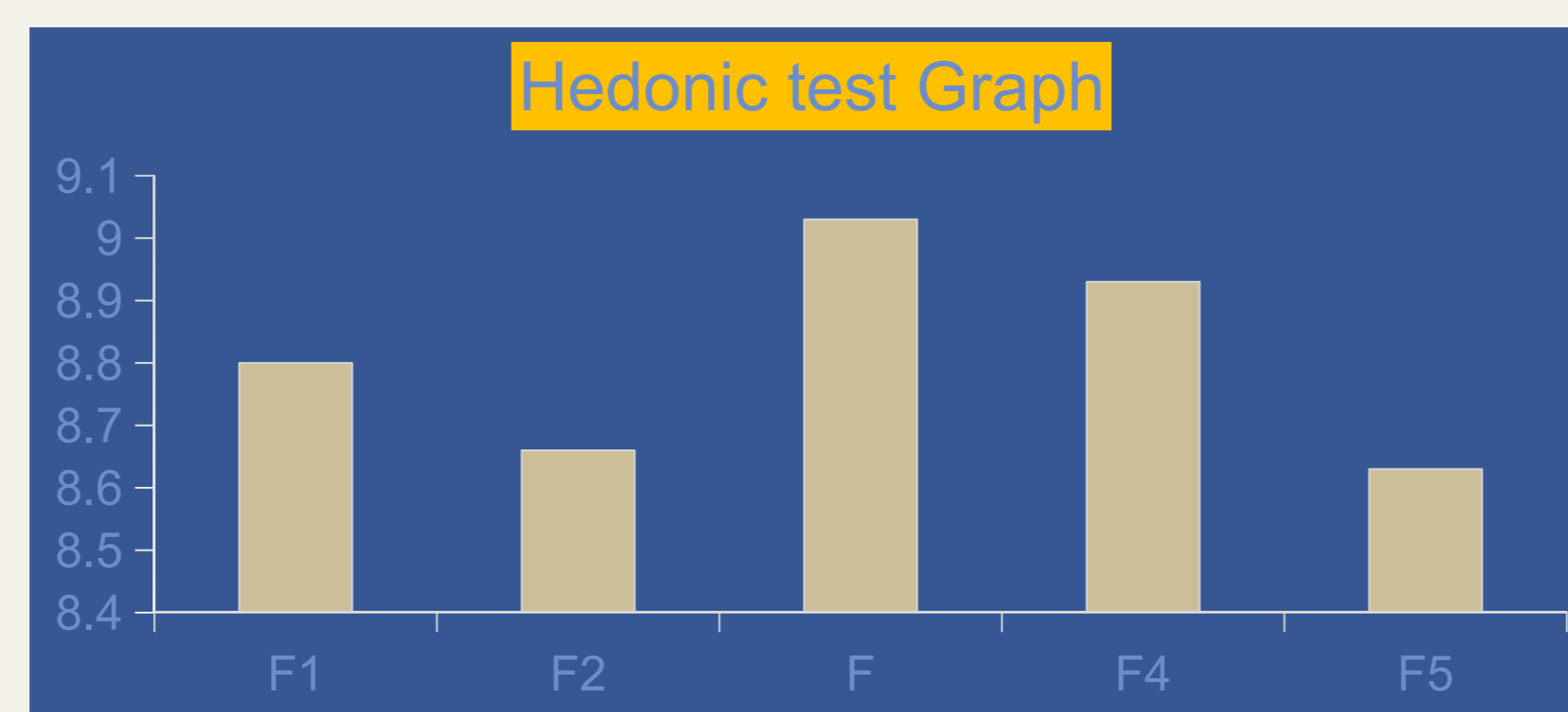
Table 1 Formula for Kopasanda Leaf Extract Chewable Tablets

Ingredient	Formulae I (50:50) (mg)	Formulae II (0:100) (mg)	Formulae III (75:25) (mg)	Formula IV (100:0) (mg)	Formula V (25:75) (mg)	Function
thick extract+ Aerosil	224 mg	224 mg	224 mg	224 mg	224 mg	active substance
Mannitol	111,75 mg	0	168 mg	223,5 mg	55,9 mg	Filler
Lactosa	111,75 mg	223,5 mg	55,9 mg	0	168 mg	Filler
PVP	20 mg	20 mg	20 mg	20 mg	20 mg	Binder
Stevia	25 mg	25 mg	25 mg	25 mg	25 mg	Sweetener
Talk	5 mg	5 mg	5 mg	5 mg	5 mg	Glidant
Mg Stearate	2,5 mg	2,5 mg	2,5 mg	2,5 mg	2,5 mg	Lubricant
Weight Per tablet	500 mg	500 mg	500 mg	500 mg	500 mg	

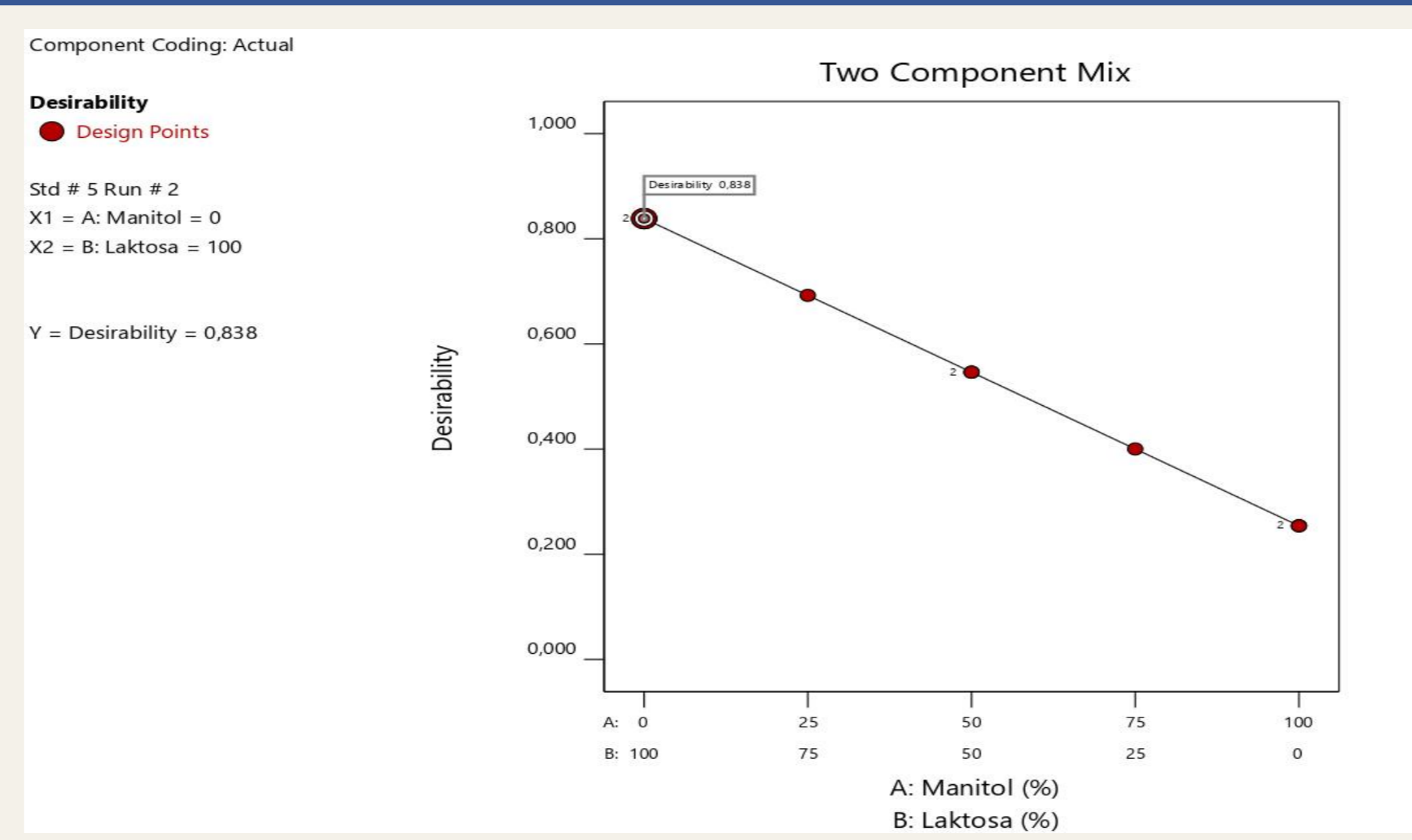
Table 2. Granule Physical Properties Evaluation Test Results

Parameter	F1± SD	F2± SD	F3± SD	F4± SD	F5± SD	Information
Flow time(second)	8,51 ± 0,77	7,51 ± 0,59	9,47 ± 0,28	8,34 ± 0,60	8,14 ± 0,62	qualify
granule angle of repose(°)	30,51± 1,27	30,80± 1,77	28,81± 0,44	31,24± 0,24	30,95± 1,10	qualify
Tapping(%)	6,66 ± 2,31	13,33± 1,15	11,33± 6,42	12 ± 2	7,33 ± 4,16	qualify

The results of all tests on the physical properties of the granules, which include tests for flow speed, angle of repose, and determination in formulas I, II, III, IV and V, have met the requirements. The physical properties of the granules are tested so that the granules can be made into tablets.



Optimum Formulas



RESULT AND DISCUSSION

Based on the results of the analysis of the response to the physical properties of the granules (flow time) and the physical properties of the tablets including hardness, disintegration time and taste response, they were included in the simplex lattice design. In this research, the optimum formula was obtained for making kopasanda leaf extract chewable tablets with a combination of mannitol and lactose fillers based on the simplex lattice design method, namely the optimum area was obtained as described in formula II, namely with a desirability value of 0.838 as the optimum formula with 0% mannitol and 100% lactose content. According to research by Mangkusari (2017), a filler ratio of 16% mannitol and 84% lactose is the optimal formula. Lactose-dominated ratios can increase granule flow properties, hardness, dissolution time, taste response and reduce the angle of repose, setability and tablet friability (Mangkusari, 2017).

Conclusion

1. The combination of Mannitol Lactose mixture can be formulated into chewable tablets which have good weight uniformity, size uniformity, hardness, friability and disintegration time and meet the requirements.
2. The results of the optimization of the simplex lattice design method using the Design Expert 12 application produced an optimum response desirability value of 0.838 at the optimum point of formula II with a combination of 0% mannitol and 100% lactose.
3. The test results of kopasanda leaf extract chewable tablet preparations showed that variations in the concentration of the filler mannitol lactose had a significant effect on the evaluation test of granule flow time, hardness, disintegration time and taste response of the tablets with a p-value < 0.05.

The stability of the flavonoid content qualitatively shows stable results, namely that the kopasanda leaf extract before and after the preparation is made still contains flavonoid compounds.

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