FORMULATION OF LOZENGES MADE FROM CARROT EXTRACt *(Daucus carota* Linn*) PRESENTED IN 1ST INTERNATIONAL CONFERENCE ON DRUG DEVELOPMENT FROM NATURAL RESOURCES*

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Abstract

Carrots were the source of â carotene which provide activities such as antioxidants to maintain health and vitamin for eyes. But the fact that most kids did not like vegetables. To increased the consumption of carrots, then th e carrots formulated become lozenges.

Preparation of carrot extract lozenges was done by direct compressed method. Granular base used in the preparation were mannitol and sucrose using binder agents with different concentration. There were PVP K-30 (1.0%, 2.0% and 3.0%) and HPMC 2910 3cps (1.0%, 1.5% and 2.0%). The granules were compressed with hydraulic press at 2 ton pressure. Physical quality of carrot extract lozenges has been evaluated, including hardness, friability and disintegration time. The formulation that having a good physical quality are granular base of manitol using PVPK-30 at 1%, 2% and 3%, granular base of sucrose using PVP K-30 2% and 3% and granular base of sucrose using HPMC 1290 3cps 2%.

Keyword : *lozenges, carrot extract, formulation*

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INTRODUCTION

â-carotene is one of carotenoids known to exist in nature, it's considered provitamins because they can be converted to active vitamin A[1]. Vitamin A is essential for normal growth and development, immune system function, and vision[2]. Â-carotenes possess antioxidant properties that help neutralise free radicals – reactive and highly energised molecules which are formed through certain normal biochemical reactions or through exogenous sources such as air pollution or cigarette smoke. Free radicals can damage lipids in cell membranes as well as the genetic material in cells, and the resulting damage may lead to the development of cancer[3,4].

Carrot (*Daucus carota* Linn.) is the best sources of á- and â-carotene, carrots are therefore high in provitamin A. The carotene content of carrots ranges from 60-120mg/100g, but some varieties can contain up to 300 mg/100g[5]. Carotenes contain mainly â-carotene, i.c. about 80%[6]. Â-carotene has been used for the prevention of vitamin A deficiency at a dose 3 to 6 mg daily for children[7].

To increase the consumption of carrots, especially children who do not like vegetables, it is necessary to innovation the carrot be lozenges. Lozenges are solid preparations that contain one or more medicaments, usually in a flavored, sweetened base, and that are intended to dissolve or disintegrate slowly in the mouth [8]. Â-carotene is an ingredient that is not stable to heat and moisture [9], therefore the manufacture of carrot extract lozenges made by direct compression. Because the dose of the carrot extract in the lozenges formulation is small, it is required excipient that will be made into granular base in the manufacture of lozenges by direct compressed method. The excipient for lozenges formulation must be sweet taste when smoked thereby sucrose (sugar) or mannitol were eligible. Sucrose is soluble in water, has a very good flow, and less hygroscopic; mannitol has a slightly sweet flavor and give sensation of cold[10].

Binder excipient which is also an important to the hardness of lozenges. This formulations used PVP K-30 or HPMC 1290 3cps with various concentrations as binding agent. PVP is able to form a strong bond between the granules, so that the resulting tablet hardness and brittleness are sufficient, it has the advantage of easily soluble in water and small concentrations of PVP K-30 is capable as a binding agent; HPMC Type 2910 is often used as a binder because it is soluble in organic solvents, inert, stable to heat, light, air and has a long chain that can form a tablet with a high hardness and low friability[10].

Based on the above, the research carried out by using sucrose or maltose as a filler agent, while the binder is used to form the granular base are PVP K-30 or HPMC 2910 cps 3 with various concentrations, then examinated the quality of the tablet that includes physical appearance, friability and the disintegrated time. From the results of this study are expected to obtain a precise formulation of the carrot extract lozenges by direct compressed method that has a good physical characteristics of the lozenges.

METHODS

Plant Material

Fresh tuberous roots of carrots (*Daucus carota* Linn.) were purchased from a vegetable market during April 2011 (Malang, Indonesia). The identity of species was confirmed by Husin RM, Director, Materia Medica Batu.

Preparation of Carrot Extract

Five kilograms fresh tuberous roots of carrots were washed with running water and cut to slices. It was dried under shade and dried root pieces were made into a coarse powder, the amount of coarse powder of carrot was 400g. The simplisia was passed through a 40-mesh sieve and extracted with aceton by percolation at room temperature[11]. The extract was concentrated with help of rotary vacuum evaporator at temperature below 35^0C.

Furthermore, concentrated extract was dried in a drying cabinet at room temperature. The percentage yield was calculated as 3.89% (15.54 g) with respect to the dried material. The extract obtained was added 6.57 g of cab-o-sil to a fine powder. The whole process should be avoid from light and heat[9].

Preparation of Base Granules

Sucrose or mannitol mixed with solution of PVP K-30 or HPMC 1290 3cps in different concentrations (Table I). The resulting granules were passed through a 12-mesh sieve, then dried in a drying cabinet with a temperature of 40-50°C to obtain granules having moisture 1-2%. Furthermore, the dried granules were passed through a 18-mesh sieve. Subsequently, the physical quality of the granular base was examinated.

Formulation of Carrot Lozenges

In this studies, the effects of various diluents and concentration of binding agents on the physical quality of carrot extract lozenges was studied by formulating tablets with mannitol or sucrose as granular base that using binder agents PVP K-30 in different concentrations of 1.0%, 2.0%, and 3.0%, and tablets with granular base of sucrose that using binder agent HPMC 1290 3cps in concentrations of 1.0%, 1.5%, and 2.0% Total weight of tablet was 700 mg. The granules were compressed in

Table I. Formulations for Granular base All weight in milligram ; *PVP* polyvinyl pyrrolidon, *HPMC* hydroxypropyl methyl cellulose

Formulation	Sucrose	PVP K-30	HPMC 2910 3cps
G1	656	1.0%	
G2	656	2.0%	
G3	656	3.0%	
G4	656	1.0%	
G5	656	2.0%	
G6	656	3.0%	
G7	656		1.0%
G8	656		1.5%
G9	656		2.0%

All weight in milligram ; *PVP* polyvinyl pyrrolidon, *HPMC* hydroxypropyl methyl cellulose

Tabel II. Tablet Formulation for Carrot Extract Lozenges Total weight of tablet 700 mg. All weight in milligrams

Formulation	Carrot Extract	Basic Granules	Magnesium Stearate
F1	37	G1 656	7
F2	37	G2 656	7
F3	37	G3 656	7
F4	37	G4 656	7
F5	37	G5 656	7
F6	37	G6 656	7
F7	37	G7 656	7
F8	37	G8 656	7
F9	37	G9 656	7

Total weight of tablet 700 mg. All weight in milligrams

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hydraulic press at 2 ton pressure with round flate faced die punches of 13.0 mm diameter and 4.5 mm thin.

All the formulations contained 37 mg of carrot extract that equivalent to 0.5 mg of â-caroteen, 656 mg of granular base as diluent and magnesium stearate (1%) was added as lubricant (Table II).

Tablets were subjected to various tests like hardness, friability and disintegration time.

RESULTS AND DISCUSSION

Evaluation of Carrot Extract Powder

The carrot extract powder was obtained from the extraction of fresh tuberous roots of carrots by percolation method using acetone. Acetone was chosen as a solvent in order to get more carotene because â-carotene dissolved in acetone. Percolation methods is used in this study because by this method the starch can not be extracted. Extraction yield from 5 kg of the fresh carrots was 15.53g and furthermore it was added with 6.57g of cab-o-sil to obtained a dry extract powder of carrot. The amount extract powder of carrot which be used was 26mg/tablet, assumed to be equal to 0.5mg â-carotene contained in fresh carrots, thereby we used 37mg dry carrot extract powder for each tablet.The whole process should be avoid from light and heat. Light and heat promote isomerisation of carotenoids. Oxidative degradation, the principal cause extensive losses of carotenoids, depends on the availability of oxygen and is stimulated by factors such as light[9].

The content of â-carotene in extract was determined spectrophotometriccaly, it was obtained that the carrot extract having $\ddot{e}_{max}$ at 448 nm as showed in Figure 1, its somewhat similar to â-carotene that's having $\ddot{e}_{max}$ at 450 nm[9]. Determination using H_2SO_4 conc. showed that the carrot extract become dark blue, it has been revealed that the carrot extract contained â-carotene[12]].

The $\ddot{e}_{max}$ of carrot extract at 448 nm, its somewhat similar to the $\ddot{e}_{max}$ of â-carotene (450 nm).

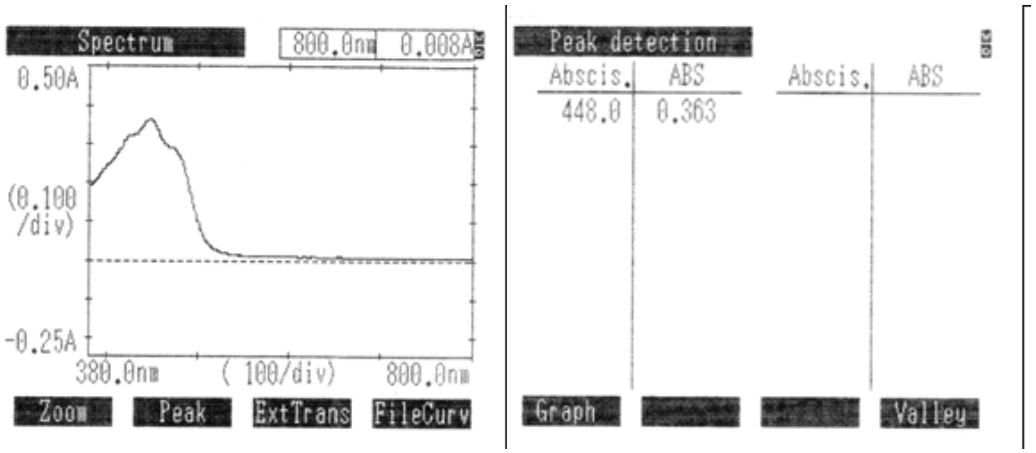

Figure 1. The absorbancy of carrot extract

Evaluation of Base *Granule*

The base granule was evaluated for moisture content, flow properties, angle of repose, loose bulk density, tapped bulk density, and compressibility index and Hausner ratio (Table III).

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Table III. Results for Evaluation of Base Granule

		Formulation				
	limits	**G1**	**G2**	**G3**	**G4**	**G5**
Moisture Content (%)[a]	1 - 2	1.20	1.74	1.26	1.09	1.12
Velocity of Flowing (g/dtk)[b]	10g/det	11.26±0.42	11.60±0.49	12.71±0.54	11.51±0.26	11.42±0.29
Angle of repose (^{o})[b]	25-40	28.30±0.42	27.82±0.43	27.57±0.43	25.64±0.93	26.26±0.54
Loose bulk density (g/ml)[b]		0.53±0.00	0.51±0.00	0.46±0.01	0.61± 0.00	0.61± 0.00
Tapped bulk density (g/ml)[b]		0.59±0.01	0.57±0.01	0.53±0.01	0.67± 0.00	0.68±0.00
Compressibility index (%)[b]		10.66±0.87	11.56±0.91	12.64±0.96	8.50±.0.80	8.82±0.00
Compactibility [1 ton (kg)[c]]		6.20±0.27	8.70±0.27	10.10±0.22	6.00±0.35	8.00±0.00
Compactibility [2 ton (kg)[c]]		9.60±0.55	10.90±0.22	12.70±0.27	7.30±0.27	9.90±0.22

		Formulation			
	limits	**G6**	**G7**	**G8**	**G9**
Moisture Content (%)[a]	1 - 2	1.22	0.92	1.04	1.02
Flow rate (g/sec)[b]	10g/det	11.65±0.69	12.29±0.18	10.52±0.12	10.35±0.17
Angle of repose (^{o})[b]	25-40	25.95±0.54	26.81±0.44	26.04±0.89	26.56±0.00
Loose bulk density (g/ml)[b]		0.62± 0.01	0.64±0.00	0.51±0.00	0.53±0.00
Tapped bulk density (g/ml)[b]		0.69±0.00	0.72±0.01	0.55±0.00	0.57±0.00
Compressibility index (%)[b]		9.66±0.83	9.41±0.79	7.27±0.00	7.00±0.00
Compactibility [1 ton (kg)]		9.10±0.22	6.80±0.45	7.20±0.55	9.20±0.45
Compactibility [2 ton (kg)]		10.80±0.27	7.60 ±0.55	8.80 ±0.45	10.00±0.00

Granular base of mannitol with PVP K-30 1.0% (G1), 2.0%(G2) and 3.0% (G3)
Granular base of sucrose with PVP K-30 1.0% (G4), 2.0% (G5) and 3.0% (G6)
Granular base of sucrose with HPMC 1290 3 cps 1.0% (G7), 1.5% (G8) and 2.0% (G9).

The values of moisture content for all formulation base granule were found to be within the limits (1.0% – 2,0%), except G7 (the granular base of sucrose using HPMC 1290 3cps 1.0% has MC 0.92%). The high level of moisture content will cause the tablet attached to the surface of the punch and die. Conversely, if the moisture content is too low, it will cause the higher of the fragility and the lozeges will be breaking easily.

Flow rate that more than 10 g/second has acceptable flow properties, whereas the flow rate for all formulation granular base were in the range 10.35 – 12.71 g/sec which indicate that the all base granules are acceptable range. Furthermore, the result for angle repose were found to be well within the limits (25^0-40^0)[13] by all formulation base granules.

Hausner ratio is calculated using measured values for bulk density ($\tilde{n}_{bulk}$) and tapped density ($\tilde{n}_{tapped}$) as follows:

$$\text{Hausner ratio} = \tilde{n}_{tapped} / \tilde{n}_{bulk}$$

Result for all formulation base granule showed in Table IV

The Hausner ratio greater than 1.25 is considered to be an indication of poor flowability. Flow character of G1, G4, G6, G8 and G9 are excellent and the other are good, thereby for all formulation of granular base are qualifying[13].

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Table IV. Hausner ratio for granular base

Formulation of granular base	Hausner ratio	Flow character
G1	1.11	Exellent
G2	1.12	Good
G3	1.15	Good
G4	1.10	Exellent
G5	1.12	Good
G6	1.11	Exellent
G7	1.13	Good
G8	1.08	Exellent
G9	1.08	Exellent

Evaluation of carrot extract lozenges

Results for hardness, friability and disintegration time are indicated in Table IV.

Table V. The Physical Quality of Carrot Extract Lozenges

Formulation	Hardness (kg)	Friability (%)	Disintegration time (minute)
F1	10.15±0.24	0.79±0.07	7.69±0.26
F2	11.10±0.21	0.57±0.01	8.40±0.07
F3	12.80±0.42	0.33±0.08	9.35±0.04
F4	8.35±0.24	0.81±0.08	6.05±0.50
F5	10.85±0.24	0.52±0.09	6.86±0.55
F6	12.55±0.37	0.29±0.01	7.74±0.57
F7	7.80±0.42	0.85±0.00	6.17±0.10
F8	9.80±0.42	0.71±0.00	6.46±0.03
F9	10.90±0.32	0.57±0.00	7.15±0.04

Lozenges which maltose base granule using PVP K-30 1.0% (F1), 2.0% (F2) and 3.0% (F3).
Lozenges which sucrose base granule using PVP K-30 1.0% (F4), 2.0% (F5) and 3.0% (F6).
Lozenges which sucrose base granule using HPMC 1290 3cps 1% (F7), 1,5% (F8) and 2.0% (F9).

The hardness of formulation of F1, F2, F3, F5, F6 and F9 were found to be well within the limits (10–20kg), whereas F4, F7 and F8 out of the limits. The influence of different of binder agent PVP K-30 to the hardness of lozenges showed that the increased of the concentration of PVP K-30 resulted to the hardness of lozenges based manitol as well as sucrose, they were tendency to rising significantly (Anova; á.<0.05). Such as those in Table V, the hardness of lozenges based sucrose with HPMC 1290 3cps increase according to the rise of HPMC 1290 3cps concentration, but only lozenges that using HPMC 2% which has a good hardness.

Friability of all formulations were in the range 0.29 – 85%. The value less 1% has a good friability[14]] which indicate that the all formulations are acceptable range. There were relationship between the hardness and friability, the more degree of hardness reduced the friability of lozenges.

The lozenges must be slow dissolved or disintegrated in the mouth . Disintegration time for all the formulations were found between 6.17 minutes and 9.35 minutes. Lozenges with disintegration time in the range 5 – 10 minutes has a good property[13], thereby disintegration time for all formulations to be well within the

limits. These results suggest that elevated levels of PVP K-30 or HPMC 1290 3 cps as a binding agent can prolong the time of disintegating tablet (Anova; á<0.05). The higher levels of the binders strengthen the bonds between the particles due to the penetration of liquid into the lozenges is more difficult and the porosity of the tablet be smaller, thereby the solubility of lozenges is longer.

CONCLUSION

Resulted from this study showed that the lozenges which made of granular base of mannitol using PVP K-30 at 1.0%, 2.0%, and 3.0%; lozenges which made of granular base of sucrose using PVP K-30 at 2.0% and 3.0 are satisfying of physical quality of lozenges and the optimal formulation of lozenges is the lozenges which granular base of mannitol using PVP K-20 1% and lozenges which granular base of sucrose using PVP K-20 2%, because using of binder agent PVP K-30 at least concentration had have satisfying of physical quality of lozenges, whereas the formulation of lozenges which made of granular base of sucrose using HPMC that meet the requirement of physical quality is losenges made of granular base of sucrose using HPMC 2%, only.

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