Jurnal Aisyah: Jurnal Ilmu Kesehatan

Volume 8, Issue 2, June 2023, p. 1181–1186
ISSN 2502-4825 (print), ISSN 2502-9495 (online)

Formulation and Physical Characteristics of Effervescent Granules from Sunkist Peels Ethanol Extract

Maya Sari Mutia[1*)], Stephanie Raibalaki[2], Siti Rahma[3], Anita Zahra[4], Ali Napiah Nasution[5], Widya Yanti Sihotang[6]

[1*), 2, 3, 4] Departement of Medicine, Faculty of Medicine, Destistry, and Health Sciences, Universitas Prima Indonesia
[5] Departement of Family Medicine, Faculty of Medicine, Destistry, and Health Sciences, Universitas Prima Indonesia
[6] Departement of Public Health, Faculty of Medicine, Destistry, and Health Sciences, Universitas Prima Indonesia

ARTICLE INFO

Article history:

Received 19 March 2023
Accepted 15 June 2023
Published 30 June 2023

Keyword:

Peels of sunkist
Extract
Effervescent
Granule

**) corresponding author*

Dr. dr. Maya Sari Mutia, M.K.M., M.Biomed

Departement of Medicine, Faculty of Medicine, Destistry, and Health Sciences, Universitas Prima Indonesia

Email: mayasarimutia@unprimdn.ac.id
DOI: 10.30604/jika.v8i2.2087

A B S T R A C T

Citrus fruit has a sweet taste and attractive shape, which is also enriched various health benefits. Some studies have been performed to investigate the pharmacology effects from the Sunkist peel extract. However, none of this study was look for the development of pharmaceutical products. Hence this study was performed to investigate the pharmaceutical formulation as an effervescent granule from Sunkist peel extract. This study was an experimental study to investigate the optimum formulation that was made by wet granulation methods. There were three formulation of Sunkist peel extract effervescent granule that were combination of organic acids (citric acid and tartaric acid), sodium bicarbonate as base compound, and some sweetener including aspartame, lactose, and mannitol. After that, the formulation was evaluated the physical properties including organoleptic, flow rate, dissolution time, foam height, pH, and angle of repose. The result of this study showed that these three formulations of Sunkist Peel extract effervescent granule showed significant different in almost all of physical properties including: flow rate (P-Value = 0.027), dissolution time (P-Value< 0.05), foam height (P-Value = 0.004), and angle of repose (P-Value: 0.043), except the degree of acidity or pH (P-Value = 0.128). Third formulation (F3) reveals the best physical properties as a Sunkist peel extract effervescent granule. Overall, it can be concluded that the third and second formulation fulfils a well physical properties of effervescent granule for Sunkist peel extract.

INTRODUCTION

Citrus fruit is one of fruits widely consumed by many people. This fruit has a sweet taste and attractive shape, which is also enriched various health benefits (Zhao et al., 2020). The increase of citrus fruit consumption found inversely associated to the incidence of some diseases (Musumeci et al., 2020). The health benefits of citrus fruit were due to the presence of bioactive compounds like phenolics (including: flavanone glycosides and hydroxycinnamic acids), vitamin C, and carotenoids (Kandemir et al., 2022; Russo et al., 2021). On the other hand, this fruit also has a source of essential oil, that was widely used for lime flavour in beverages, cake, or some desserts. Some studies has been reported that this essential oil has antioxidant properties of citrus (Kandemir et al., 2022).

The fruit peels have been used for many purposes. However, the fruit peel becomes a wasted product, that has a potential to become a nutraceutical product (Zia et al., 2021). Due to their low cost and easily obtained, the Sunkist peels are able to offer a significant low-cost nutritional food supplement. Utilization of this bioactive-rich citrus residue can provide an efficient, inexpensive, and environmentally friendly platform for the production of new nutraceuticals or for upgrading existing ones (Ali & Imran, 2021; Sari et al., 2021).

Some previous studies have been performed to look for the pharmacology effects from the Sunkist peel extract.

Suhartomi et al. (2019) have been reported that both orange peel extract and fraction enriched by flavonoid, that was responsible for its antioxidant activity (Suhartomi et al., 2019). Mutia et al (2019) has been reported the hepatoprotective effect from the Sunkist peels extract from the Paracetamol-induce liver injury (Mutia & Chiuman, 2019). Furthermore, Mutia et al. (2021) also reported that Sunkist peel ethanol extract has an antidiabetic effect that was also kidney protection effect from the diabetic nephropathy as the long-term complications (Sari et al., 2021). However, these previous studies used the extract as a oral suspension, that was made of sodium carboxymethylcellulose and this oral suspension was made without any physical, chemical, or microbiology formulation control (Cirri et al., 2020). It becomes important to develop a easily applied pharmaceutical product from Sunkist Peel ethanol extract. Thus, this study was used to look for the effervescent granule formulation for Sunkist peels extract and this study also evaluate the physical properties of this effervescent granule.

Table 1. Formulation of Sunkist Peel Extract Effervescent Granule

Material	1st Formula (%)	2nd Formula (%)	3rd Formula (%)
Sunkist peel extract	12	4.3	9.89
PVP	3	2.5	4.5
Sodium Bicarbonate	30	15	35
Aspartame	0.7	1.4	2.5
Mannitol	35	20	30
Lactose	0	12	15
Citric Acid	10	4	5
Tartrate Acid	20	15	25

METHODS

Materials

This study was an experimental study that was performed in Pharmacology Laboratory, Faculty of Medicine, Dentistry, and Health Sciences, Universitas Prima Indonesia at October 2022 – December 2022. This study used some instrument including blender, mesh sieves no. 12 and no. 14, rotary evaporator, laboratory water bath, drying cabinet, stopwatch, analytic scale, ovens, flow tester, spatula, mortar and pestle, beaker glass, test tube, volumetric flask, and Erlenmeyer. On the other hand, some materials that was also used in this study including Sunkist peel, citric acid, tartaric acid, sodium bicarbonate, mannitol, aspartame, flavour, PVP, and 96% Ethanol solution.

Methods

Initially, Sunkist fruit was obtained from a traditional market in Pancurbatu district in Medan Town, North Sumatera, Indonesia. All Sunkist fruits were peel off and the Sunkist peel was collected to wash. After that, Sunkist peel was weighed and dried in drying cabinet, then the dried Sunkist peel was blended with blender to form a simplicial powder. This simplicial powder was soaked into 96% ethanol solution for maceration for four days and it was filtered to obtain the filtrate. Finally, this filtrate was evaporated by rotary evaporator and water bath to form a concentrated Sunkist peel extract. The obtained Sunkist peel extract was used to form effervescent by granulation methods. The formulation of effervescent granule was described in Table 1.

Organoleptic

Organoleptic evaluation was performed to evaluate the color, odor, and taste of Sunkist peel effervescent granule. Taste and color were narratively describe, meanwhile the odor was express as semi-quantitative scale (0: No to minimal odor; +: Mild odor; ++: Moderate odor; +++: Strong odor).

Flow rate

Seven grams of Sunkist Peels effervescent granule was put in to a funnel fixed-to-a-stand. After that, the flow rate was obtained by divided the mass of granule that was used for this test into the duration of granule to set up until drop.

Angle of repose Sunkist peel extract effervescent granule was made by wet granulation method. Initially, all acid components including citric acid, tartaric acid, and Sunkist peel extract was mixed and occasionally stirred. On the other hand, PVP (Polyvinylpyrrolidone) were gradually added by sufficient quantity of distilled water u

Angle of repose was performed after flow rate evaluation. The dropped Sunkist peels effervescent was measured the angle between the double height of dropped granule and the distance of dropped granule.

Dissolution Time

Seven grams of Sunkist peels effervescent granule was dissolved into twelve-millimetres distilled water. Then, the dissolution time defined as a required time of granule to completely dissolve in the distilled water and it was expressed as a minute.

Foam Height

Foam height was evaluated after the granule was dissolve into twelve-millimetres distilled water and it was expressed as centimetres (cm).

Degree of acidity

On the other hand, the dissolved Sunkist peels granule was also measured the degree of acidity by digitalized pH meter.

RESULTS AND DISCUSSION

This study was used Sunkist Orange from a traditional market in Medan city and it was extracted by maceration method. The obtained extract was showed some physical parameters which was described in Table 2.

Table 2. Characteristics of Sunkist Peel Extract

Characteristics	Value
Fresh simplicial weight (gr)	64,000
Dry Simplicia Powder Weight (gr)	682.16
Solvent Volume (ml)	7,000
Extract Weight (gr)	118.38
Yield (%)	17.35

Based on Table 2 above it can be seen that 682.16 grams of Sunkist peels powder was extracted and formed 118.38 gram of concentrated Sunkist peels extract. Thus, the yield of the Sunkist peel extract was 17.35%. The obtained Sunkist peels extract was formulated into Sunkist peel extract granule and underwent physical characteristic evaluation. The organoleptic from the Sunkist Peel extract granule was described in Table 3.

Table 3. Organoleptic properties of Sunkist Peel Extract Effervescent Granule

Organoleptic	F1	F2	F3
Taste	Bitter	Little bit sweet	Sweet
Smell	+++	++	+
Colour	Brownish Yellow	Yellow	Yellow

Table 4. Physical Properties of Sunkist Peel Extract Effervescent Granule

Physical Properties	F1	F2	F3	P-Value
Flow Rate (gr/ s)	1.20 (1.20-1.30)	4.70 (4.40-4.80)	5.00 (4.90-5.10)	0.027*
Dissolution Time (minutes)	2.82 ± 0.11	2.16 ± 0.04	2.63 ± 0.10	< 0.05**
Foam Height (cm)	3.63 ± 0.15	2.77 ± 0.25	3.03 ± 0.15	0.004**
pH	4.87 ± 0.25	4.43 ± 0.25	4.57 ± 0.15	0.128**
Angle of repose (θ)	37.90 (37.00-41.30)	17.70 (16.30-19.60)	21.10 (17.70-21.10)	0.043*

*p-value was obtained from Kruskal-Wallis; ** p-value was obtained from One Way ANOVA

Based on Table 3, it can be seen that the Sunkist Peel extract effervescent granule from first, second, and third formulation have a bitter, little bit sweet, and sweet taste, respectively. Smell of these first, second, and third formulation were mild, moderate, and strong odor, respectively. Finally, the colour of first formulation was brownish yellow and the second and third formulation were yellow. This study also evaluated others physical properties that was described in Table 4.

Based on Table 4 above, it can be seen that these three formulations of Sunkist Peel extract effervescent granule showed significant different in almost all of physical properties including: flow rate (p-value = 0.027), dissolution time (p-value< 0.05), foam height (p-value = 0.004), and angle of repose (p-value: 0.043), except the degree of acidity or pH (p-value = 0.128). Third formulation (F3) reveals the best physical properties as a Sunkist peel extract effervescent granule. The flow rate, dissolution time, foam height, pH, and angle of repose from third formulation were 5.00 (4.90-5.10) gram/second, 2.63 ± 0.10 minutes, 3.03 ± 0.15 cm, 4.57 ± 0.15, and 21.10 (17.70-21.10) degree, respectively. Meanwhile, the reference value of flow rate, dissolution time, foam height, pH, and angle of repose were less than 10 gram/ second, < 5 minutes, 3.00 cm, 6.00-7.00, and < 30o, respectively.

This study used maceration methods for extraction process and the result showed the yield extract of 17.35%. The yield extract was used to evaluate the quality of extract, higher yield extract indicates the lower the quality of extract. Some previous studies have been reported the yield extract of orange, that was in line with the result of this study. Lubis et al. (2021) reported that the yield of Methanol Sunkist peel extract was 22.38% (Lubis & Mutia, 2021). On the other hand, Gulo et al. (2021) also reported that the yield of ethanol and ethyl acetate orange peel extract were 19.49% and 5.45%, respectively (Gulo et al., 2021). The variation of these yield value can be affected by some factor including Polarity of solvent and duration of maceration. Increased the polarity of solvent also increases the yield value and decrease the quality of extract. Thus, it become obvious that the less polarity solvent may improve the quality of extract. Effervescent granule is an oral pharmaceutical that was formulated by combination of organic acids and base compound. These organic acids were citric acids and tartaric acid, which was acts as acid salts. When the formulation used single acid component, it may cause instable granule effervescent that can be either the extract to easily underwent effervescent or form a sticky mixture. On the other hand, these acid compounds may also strengthen bonds between the particles in the effervescent granule. Meanwhile, the sodium bicarbonate was used to react with these organic acids to improve the taste and induce the effervescent reaction. The effervescent reaction was a chemical reaction between the sodium bicarbonate and organic compounds, which liberate a carbon dioxide gas as bubbles and a refreshing sparkle effect. This formulation also used other sweeteners like aspartame, lactose, and mannitol to improve the taste of effervescent granule. Finally, this formulation used Polyvinylpyrrolidone (PVP) as binder to form a granule. This compound was an inertness, non-toxicity, and biocompatibility compound in delivery systems of effervescent granule (Grajang & Wahyuningsih, 2018; Wati & Saryanti, 2019).

The flow rate and angle of repose in this study was affect by shape, size, porosity, density, and particle frictional forces. The citric acid, tartaric acid, and PVP compound was responsible for the flow rate and angle of repose. The high citric acid level may also increase the tendency of this formulation become sticky and decrease the flowability of granule (Da, 2022; Zhou et al., 2022). On the other hand, the higher PVP level may increase the binder between the particle decrease the tendency of particle to move freely in the flow funnel and it cause to increase the flow rate and reduce the angle of repose (Wati & Saryanti, 2019; Wen et al., 2018). This study was also used the tartaric acid as the acid compounds, which has the higher molecular density than the citric acid. Thus, both citric acid and tartaric acid increase the molecular

weight of effervescent granule and accelerate the drop of granule from the flow funnel by gravitation force.

This study was showed that the highest flow rate was shown in third formulation, which due to the high density of tartaric acid that was used than other formulation. Even thought, the first formulation also used similar level of these organic compounds to third formulation, but the third formulate has higher level of tartaric acid than the first formulation. Meanwhile, the first formulation showed the highest angle of repose and this value higher than the reference value, it may due to the high level of citric acid that caused the granule become sticky and difficult to form a narrower angle of repose than other formulation with lower citric acid level. Polyvinylpyrrolidone also has hygroscopic properties to absorb water and facilitate the effervescent reaction between the sodium bicarbonate and organic acids to liberate carbon dioxide (CO2). The effervescent reaction was a reaction between sodium bicarbonate soluble against either organic compound in water to form a salt product, water, and carbon dioxide by enhancing the water penetration into the granule. Thus, the increase PVP level also accelerates the dissolution time of granule effervescent. Meanwhile, the increase the number of carbon dioxide gas as the result of effervescent reaction was affects by the concentration of organics acids and base compounds as the reactants.

This study showed that the fastest dissolution time was found in second formulation and the slowest one was first formulation. It may due to the level of reactant including sodium bicarbonate, citric acid, and tartaric acid. The ratio of acid and sodium bicarbonate in the first (30:30) and third formulation (30: 35) were higher that the second formulation (19: 15). In this study, the sodium bicarbonate was act as a limiting reactant, so when the acid compound was higher than or similar to base compound, the excessive acid cannot be reacted to the base because the base compound was less. However, this study showed that the first and third formulation had higher foam height than the second formulation. It may due to the higher level of sodium bicarbonate containing carbon dioxide in first and third formulation.

LIMITATION OF THE STUDY

This study has limitations. The design used in collecting data only measure the formulation of effervescent granule of the extract. This extract need to be test in vivo study.

CONCLUSION

Overall, it can be concluded that the third and second formulation fulfils a well physical properties of effervescent granule for Sunkist peel extract. The third formulation has the best physical properties with The flow rate of 5.00 (4.90-5.10) gram/second, dissolution time of 2.63 ± 0.10 minutes, foam height of 3.03 ± 0.15 cm, pH of 4.57 ± 0.15, and angle of repose of 21.10 (17.70-21.10) degree.

ETHICAL CONSIDERATIONS

Funding Statement

There was no support from any organization for this study.

Conflict of Interest Statement

There is no conflicts of interest in this study.

REFERENCES

Ali, A., & Imran, M. (2021). Remotely sensed real-time quantification of biophysical and biochemical traits of Citrus (Citrus sinensis L.) fruit orchards – A review. *Scientia Horticulturae*, *282*, 110024. https://doi.org/10.1016/j.scienta.2021.110024

Cirri, M., Maestrelli, F., Mennini, N., Di Cesare Mannelli, L., Micheli, L., Ghelardini, C., & Mura, P. (2020). Development of a stable oral pediatric solution of hydrochlorothiazide by the combined use of cyclodextrins and hydrophilic polymers. *International Journal of Pharmaceutics*, *587*, 119692. https://doi.org/10.1016/j.ijpharm.2020.119692

Da, R. (2022). *Potential Granule Effervescent from a mixture of beetroot extract (Beta vulgaris L), Malang apple (Malus sylvestris L .) and Carrot (Daucus carota L .) as Preparation for Lowering Blood Cholesterol Levels*. *7*(2), 934–938.

Grajang, I. B., & Wahyuningsih, I. (2018). Formulation of Sechium edule Extract Effervescent Granule with the Variation of Citric Acid, Tartrate Acid and Sodium Bicarbonate. *Proceedings of the 1st Muhammadiyah International Conference on Health and Pharmaceutical Development*, 54–60. https://doi.org/10.5220/0008239300540060

Gulo, K. N., Suhartomi, Saragih, A. D., Raif, M. A., & Ikhtiari, R. (2021). Antioxidant Activity of Flavonoid Compounds in Ethanol and Ethyl Acetate Extract from Citrus Sinensis. *2021 International Conference on Artificial Intelligence and Mechatronics Systems (AIMS)*, 1–6. https://doi.org/10.1109/AIMS52415.2021.9466078

Kandemir, K., Piskin, E., Xiao, J., Tomas, M., & Capanoglu, E. (2022). Fruit Juice Industry Wastes as a Source of Bioactives. *Journal of Agricultural and Food Chemistry*, *70*(23), 6805–6832. https://doi.org/10.1021/acs.jafc.2c00756

Lubis, Y. E. P., & Mutia, M. S. (2021). Liver Protection Activity of Sunkist Orange (Citrus sinensis L. Osbeck) Peels in Cyclophosphamide Induced Male Wistar Rat. *2021 IEEE International Conference on Health, Instrumentation & Measurement, and Natural Sciences (InHeNce)*, 1–5. https://doi.org/10.1109/InHeNce52833.2021.9537213

Musumeci, L., Maugeri, A., Cirmi, S., Lombardo, G. E., Russo, C., Gangemi, S., Calapai, G., & Navarra, M. (2020). Citrus fruits and their flavonoids in inflammatory bowel disease: an overview. *Natural Product Research*, *34*(1), 122–136. https://doi.org/10.1080/14786419.2019.1601196

Mutia, M. S., & Chiuman, L. (2019). Hepatoprotective Effect of Citrus sinensis (L.) Osbeck Ethanol Extract in Paracetamol-Induced Rats. *Majalah Kedokteran Bandung*, *51*(4), 189–193. https://doi.org/10.15395/mkb.v51n4.1794

Russo, C., Maugeri, A., Lombardo, G. E., Musumeci, L., Barreca, D., Rapisarda, A., Cirmi, S., & Navarra, M. (2021). The Second Life of Citrus Fruit Waste: A Valuable Source of Bioactive Compounds. *Molecules*, *26*(19), 5991. https://doi.org/10.3390/molecules26195991

Sari, M., Ginting, C. N., & Yulizal, O. (2021). Sunkist Peel Ethanol Extract Ameliorates Diabetic Nephropathy in Streptozotocin-Induced Diabetic Wistar Rats. *Open Access Macedonian Journal of Medical Sciences*, *9*(A), 1086–1091. https://doi.org/10.3889/oamjms.2021.7362

Suhartomi, ., Gulo, K. N., Saragih, A. D., Martinus, A. R., & Ikhtiari, R. (2019). Antioxidant Properties of Sweet Orange Peels in Several Fractions of Methanolic Extract. *Proceedings of the International Conference on Health Informatics and Medical Application Technology*, 371–378. https://doi.org/10.5220/0009515503710378

Wati, S., & Saryanti, D. (2019). Effervescent Granule Formulation of Bitter Melon Extract (Momordica charantia L.) with Gelatin as A Wet Granulation Binder. *Journal of Nutraceuticals and Herbal Medicine*, *2*(1), 20–28. http://journals.ums.ac.id/index.php/jnhm

Wen, J., Liu, W., Xie, Z., Lou, C., & Yang, X. (2018). Effects of PVP incorporation on the properties of injection-molded high-performance ceramics with PEG-based binders. *Ceramics International*, *44*(3), 2718–2726. https://doi.org/10.1016/j.ceramint.2017.10.227

Zhao, L., Wang, K., Wang, K., Zhu, J., & Hu, Z. (2020). Nutrient components, health benefits, and safety of litchi (Litchi chinensis Sonn.): A review. *Comprehensive Reviews in Food Science and Food Safety*, *19*(4), 2139–2163. https://doi.org/10.1111/1541-4337.12590

Zhou, H., Tian, X., Guo, X., Kou, M., Wu, S., Shen, Y., & You, Y. (2022). DEM study of the angle of repose and porosity distribution of cylindrical particles with different lengths. *International Journal of Chemical Reactor Engineering*, *20*(2), 197–207. https://doi.org/10.1515/ijcre-2021-0174

Zia, S., Khan, M. R., Shabbir, M. A., & Aadil, R. M. (2021). An update on functional, nutraceutical and industrial applications of watermelon by-products: A comprehensive review. *Trends in Food Science & Technology*, *114*, 275–291. https://doi.org/10.1016/j.tifs.2021.05.039