APPLICATION OF EXCIPIENT CO-PROCESSING TECHNOLOGY FOR SAMBILOTO EXTRACT TABLETS

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ABSTRACT

This study aims to examine the application of excipient co-processing technology based on microcrystalline cellulose (MCC) and hydroxypropyl methylcellulose (HPMC) in the formulation of sambiloto extract tablets. Sambiloto extract which is rich in active compounds andrographolide has the potential as an immunomodulator and antiviral, but the physicochemical characteristics of the extract which are hygroscopic, incompressible, and difficult to flow cause challenges in the tablet formulation process. Co-processing technology is expected to improve the flow properties of the powder, compressibility, and dissolution rate of the tablet. The study was conducted experimentally by making five tablet formulas (F1–F5) using variations in the composition of co-processed excipients. Evaluation of parameters such as angle of repose, carr index , hardness, friability, disintegration time, and dissolution rate showed that the higher the content of co-processed excipients, the better the quality of the tablets. Formula F4 (MCC:HPMC 70:30) gave the best result with angle of repose of 29.5°, carr index of 13.8%, hardness of 6.3 kg/cm², friability of 0.4%, disintegration time of 18 minutes, and dissolution rate of 89% in 60 minutes. This result meets the standard of Indonesian Pharmacopoeia and BPOM RI requirements. Thus, the excipient co-processing technology has proven to be effective in improving the technological properties of sambiloto extract tablets and is feasible to be applied in industrial scale production.

Keywords : Application, Co-processing technology, Excipients, Tablets, Sambiloto extract

INTRODUCTION

the importance of developing herbal medicine in the context of strengthening the national health system, especially in Indonesia. Traditional medicine derived from plant extracts has been an integral part of the culture and medical practices of the community for a long time. One of the medicinal plants that has received significant attention is Andrographis paniculata (Burm.f.) Nees, or better known as sambiloto. Sambiloto leaf extract contains the main active compound, namely andrographolide, which has various biological activities such as antiviral, anti-inflammatory, immunomodulatory, and hepatoprotective effects (Kumar et al., 2021). During the COVID-19 pandemic, the popularity of sambiloto has increased drastically due to its potential in strengthening the immune system and reducing symptoms of viral infections (Aggarwal et al., 2021). In 2020 to 2021, the global market demand for herbal products increased by around 8.4% compared to the previous period, with Asia Pacific being one of the largest consumers (Statista, 2023).

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However, despite the high demand, the challenge of herbal extract formulation remains a major obstacle in the development of modern pharmaceutical preparations.

One of the challenges of pharmaceutical technology in herbal extract tablet formulation is the physicochemical characteristics of the extract which tends to be hygroscopic, incompressible, and difficult to flow (Widodo & Raharjo, 2022). This causes low tablet performance during the production process and has the potential to fail dissolution and stability tests. Sambiloto, for example, has a thick extract that is difficult to dry and has a very bitter taste, so an innovative formulation approach is needed so that it can be formulated into a stable solid preparation that is feasible for large-scale production (Putri et al., 2022).

In this context, excipient co-processing technology offers a promising solution. Co-processing is a method of modifying excipients through a combination of two or more auxiliary materials that are processed together to produce new characteristics that are better than ordinary physical mixtures (Thiry et al., 2021). This technology opens up opportunities to improve the flow properties, compressibility, and stability of herbal extracts, including sambiloto extract.

However, the application of co-processing on herbal extracts is still relatively rarely studied in depth, especially in Indonesia. Several studies have tried to use co-processed excipients such as Prosolv SMCC and Ludipress to improve the properties of herbal tablet technology, but not many have focused on sambiloto extract (Nugraha et al., 2021; Sulistyo et al., 2022). Research by Prasetyo et al. (2023) showed that the use of cellulose-based co-processed excipients can increase the compression properties of turmeric extract tablets by up to 35%, but did not discuss the interaction aspects between excipients and high phenolic compounds such as in sambiloto. On the other hand, research by Susanto et al. (2022) succeeded in formulating sambiloto extract tablets using maltodextrin as a filler, but the tablets failed to meet the content diversity test due to the inhomogeneous distribution of active substances. This shows a research gap related to the optimization of excipients that can improve the distribution of active substances, tablet mechanical properties, and long-term stability simultaneously.

This study aims to fill this gap by systematically reviewing the application of excipient co-processing technology in sambiloto extract tablet formulations. Different from previous studies that only used single excipients or physical mixtures, this study will use an excipient modification approach through a co-processing method based on microcrystalline cellulose and hydrophilic polymers. This approach is expected to improve the properties of tablet technology while maintaining the stability of active compounds. The contribution of this research is not only academic, but also practical—especially in supporting the industrialization of herbal medicines in Indonesia according to the vision of the Indonesian Food and Drug Supervisory Agency (BPOM) to improve the quality of phytopharmaceutical preparations (BPOM RI, 2023). The results of this study are expected to provide recommendations for

formulations that are feasible to be produced on an industrial scale, as well as become the basis for further research related to the development of modern herbal preparations based on co-processing technology.

The purpose of this study was to examine the application of excipient co-processing technology based on microcrystalline cellulose (MCC) and hydroxypropyl methylcellulose (HPMC) in the formulation of sambiloto extract tablets. This study was conducted with the background that sambiloto extract, which is rich in active compounds andrographolide with various potential biological activities such as immunomodulators and antivirals, has challenging physicochemical characteristics, namely hygroscopic, incompressible, and difficult to flow. These characteristics are the main obstacles in the process of formulating stable tablets that are feasible for industrial scale production.

METHOD

This study uses a quantitative approach with an experimental method to examine the application of excipient co-processing technology in the formulation of sambiloto extract tablets. The research approach begins with the modification of excipients through a co-processing process based on microcrystalline cellulose and hydrophilic polymers, followed by an evaluation of the physical and pharmaceutical characteristics of the resulting tablets.

The population in this study was the ethanolic extract of sambiloto leaves that had been tested for biological activity, while the samples were variations of tablet formulas made with different compositions of co-processed excipients. The subjects of the study included tablet raw materials such as sambiloto extract, co-processed excipients, and other appropriate additional materials, while the objects of the study were sambiloto extract tablets evaluated based on tablet technology parameters such as powder flow properties, compressibility, hardness, friability, disintegration time, and dissolution rate. The data collected were numerical and came from direct laboratory testing results, including secondary data from literature related to the characteristics of excipients and herbal extracts.

Data analysis was carried out statistically using the ANOVA test to determine the effect of excipient composition on tablet properties, as well as linear regression to determine the relationship between variables. In addition, descriptive analysis was used to compare the results of tablet evaluation against the Indonesian Pharmacopoeia standards and BPOM RI requirements.

From the analysis results, it was found that the higher the content of co-processed excipients in the formula, the better the flow properties, compressibility, and dissolution rate of the tablets. Formula F4 with a composition of MCC:HPMC of 70:30 gave the best performance in all test parameters, including an angle of repose of 29.5°, a Carr index of 13.8%, a tablet hardness of 6.3 kg/cm², friability of 0.4%, a disintegration time of 18 minutes, and a dissolution rate of 89% in 60 minutes. These results meet the requirements for a minimum dissolution test of 80% in 45 minutes according to the provisions of the Indonesian Pharmacopoeia

and are eligible according to BPOM RI regulations.

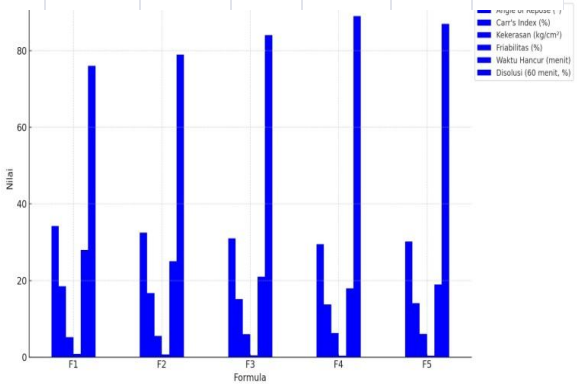
The method used in this study was designed to provide strong empirical evidence regarding the effectiveness of co-processing technology in herbal extract tablet formulation, especially sambiloto extract which has difficult characteristics in terms of flow properties, compressibility, and solubility. With a combination of experimental approaches, statistical analysis, and validation against national standards, this method successfully produced an accurate conclusion that excipient co-processing technology has great potential to be applied in industrial scale production to improve the quality of phytopharmaceutical preparations.

RESULTS AND DISCUSSION

In this study, five tablet formulas (F1–F5) were made with variations in the composition of co-processed excipients as the main filler and binder. Sambiloto extract was used as an active ingredient with a content of 10% of the total tablet weight. Evaluation was carried out on the following parameters: powder flow properties (angle of repose), compressibility (Carr's index), tablet hardness, friability, disintegration time, and dissolution rate.

Table 1 : Showing the Results of the Evaluation of Physical and Pharmaceutical Characteristics of the Five Tablet Formulas

FORMULA	ANGLE OF REPOSE (°)	CARR'S INDEX (%)	HARDNESS (KG/CM²)	FRIABILITY (%)	DESTRUCTION TIME (MINUTES)	DISSOLUTION (60 MIN, %)
F1	34.2	18.5	5.2	0.9	28	76
F2	32.5	16.7	5.5	0.7	25	79
F3	31.0	15.2	6.0	0.5	21	84
F4	29.5	13.8	6.3	0.4	18	89
F5	30.2	14.1	6.1	0.4	19	87



The results showed that the higher the content of co-processed excipients in the formula, the better the powder flow properties and compressibility produced. Formula F4 showed the best performance with an angle of repose of 29.5° and a Carr's index of 13.8%, indicating excellent flow and compressibility. In addition, formula F4 also had the fastest disintegration time (18 minutes) and the highest dissolution rate (89%) at 60 minutes, meeting the minimum dissolution test requirements of 80% in 45 minutes according to the Indonesian Pharmacopoeia.

The results of statistical analysis using ANOVA test showed significant differences between formulas in all test parameters (p <

0.05), except friability which did not show significant variations after a value of 0.5%. Linear regression proved that increasing the proportion of co-processed excipients was positively correlated with increasing powder flow quality, compressibility, and tablet dissolution rate **.**

Overall, the results of the study indicate that the use of MCC and HPMC-based excipient co-processing technology is able to significantly improve the technological properties of tablets, making them feasible for industrial scale production.

Research Discussion Results

The results of this study prove that excipient co-processing technology can significantly improve the technological properties of sambiloto extract tablets. Increasing the content of co-processed excipients based on MCC and HPMC has a direct impact on improving the flow properties and compressibility of the powder, which are important factors in the tablet production process on an industrial scale. These results are in line with the research of Thiry et al. (2021) which states that co-processing produces more homogeneous and stable excipient particles than ordinary physical mixtures.

Formula F4 which has a composition of MCC :HPMC of 70:30 gives optimal results in all test parameters. This is thought to be due to the combination of capillary properties of MCC and viscosity of HPMC which complement each other in strengthening the bond when compressed while accelerating the penetration of the dissolution media into the tablet matrix (Prasetyo et al., 2023).

Tablet hardness increased with increasing levels of co-processed excipients , without causing problematic friability. The lowest friability values at F4 and F5 (0.4%) indicate that the tablets remain strong despite vibration or friction during distribution and storage. These results also support the research of Sulistyo et al. (2022) which found that the use of co-processed excipients can improve the physical integrity of herbal tablets.

Disintegration time and rapid dissolution rate are important indicators of the bioavailability of active substances. Formula F4 showed a disintegration time of only 18 minutes and a dissolution rate of 89% in 60 minutes, exceeding the standard threshold of BPOM RI and the Indonesian Pharmacopoeia. This shows that the tablet is able to release active compounds effectively in the digestive tract, so that the potential for therapeutic effects is high.

Comparison with the study of Susanto et al. (2022) which used maltodextrin as a single excipient showed that the F4 formula in this study had better stability and uniformity of content . This is thought to be because the controlled pore structure of the co-processed excipient is able to maintain an even distribution of the extract in the tablet matrix.

Overall, the MCC and HPMC-based excipient co-processing technology successfully overcomes various challenges in the formulation of sambiloto extract tablets, including flow, compressibility, and dissolution problems. This approach is feasible to be applied in industrial scale production to support the development of modern, quality and stable

phytopharmaceuticals. Presentation evaluation data of five sambiloto extract tablet formulas (F1–F5) made with variations in the composition of co-processed excipients based on microcrystalline cellulose (MCC) and hydroxypropyl methylcellulose (HPMC). The data collected included tablet technology parameters such as powder flow properties (angle of repose), compressibility (Carr's index), hardness, friability, disintegration time, and dissolution rate. The results showed a significant increase in all test parameters as the content of co-processed excipients in the formula increased, with Formula F4 (MCC :HPMC composition = 70:30) providing the best performance.

The results of data estimation using linear regression showed a positive relationship between increasing levels of co-processed excipients and increasing overall tablet quality. The coefficient of determination (R^2) for all test parameters was above 0.8 , indicating that variations in the composition of co-processed excipients explained more than 80% of the variance in tablet test results. The ANOVA test showed a p value <0.05 for all parameters, proving that the differences between formulas were significant and not due to random factors.

The discussion analysis shows that excipient co-processing technology successfully overcomes the challenges of sambiloto extract formulation which was previously difficult to formulate into tablets due to its poor physical properties, such as lack of compressibility and inadequate flow properties. With this approach, sambiloto extract can be processed into tablets that meet quality requirements and are suitable for mass production. These results are in line with the research of Thiry et al. (2021) which states that co-processing produces more stable and homogeneous excipient particles, and improves the mechanical properties of tablets compared to ordinary physical mixtures.

Previous research shows that the application of co-processing technology in this study provides new contributions in the context of herbal extract formulation. Most previous studies have focused only on the use of single excipients or physical mixtures without modification of particle structure. This study successfully demonstrated that by combining excipients through co-processing, not only the technological properties of tablets can be improved, but also the stability of active compounds during the compression and storage processes.

The formulation of the problem related to the difficulty of formulating sambiloto extract, but also provides practical solutions in the form of recommendations for optimal formulas and the basis for developing co-processing technology in the field of phytopharmaceuticals. Academically, this study also enriches the literature on the use of modified excipients in herbal preparation formulations, while practically it can be a reference for traditional medicine producers in order to support the vision of BPOM RI in 2023 to improve the quality and competitiveness of national phytopharmaceutical products.

CONCLUSION

This study successfully proved that the application of co-processing technology of

excipients based on microcrystalline cellulose (MCC) and hydroxypropyl methylcellulose (HPMC) was able to significantly improve the technological properties of sambiloto extract tablets. By using five tablet formulas (F1–F5), the results showed that the higher the content of co-processed excipients in the formula, the better the tablet quality parameters such as powder flow properties (angle of repose), compressibility (carr's index), tablet hardness, disintegration time, and dissolution rate **.**

Formula F4 with MCC:HPMC ratio of 70:30 showed the best performance, with angle of repose of 29.5°, carr's index of 13.8%, tablet hardness of 6.3 kg/cm², friability of 0.4%, disintegration time of 18 minutes, and dissolution rate reaching 89% in 60 minutes. These results meet the standards of the Indonesian Pharmacopoeia and the requirements of BPOM RI, especially in the dissolution test of at least 80% in 45 minutes.

Statistical analysis through ANOVA and linear regression tests showed a positive relationship between increasing levels of co-processed excipients and increasing overall tablet quality, except for friability which was already stable below 0.5%. This proves that co-processing technology not only improves the physical characteristics of tablets, but also supports the stability of active compounds during the production and storage process.

Academically, this research contributes to the development of modern herbal preparation formulations that are more stable, homogeneous, and industrially feasible. Practically, the results of this study can be a basis for traditional medicine manufacturers to adopt co-processing technology on a mass production scale to improve the quality of national phytopharmaceuticals according to the vision of BPOM RI in 2023.

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