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Research Article

Formulation and Evaluation of Antioxidant Activity of Instant Granules from 70% Ethanol Extract of Single Black Garlic (*Allium sativum* L.)

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Abstract

Free radicals contribute to various diseases by inducing oxidative stress. Single black garlic (*Allium sativum* L.) is recognized for its phenolic compounds, which possess radical-scavenging properties. This study aimed to develop and evaluate instant granules containing black *A. sativum* extract for their antioxidant activity and physicochemical characteristics. An instant granule formulation was developed using a 70% ethanol extract of a single black *A. sativum*, with three distinct formulas containing 5%, 7.5%, and 10% extract (Formulas 1, 2, and 3, respectively). The granules were subjected to comprehensive physical quality assessments, including organoleptic properties, moisture content, angle of repose, flow rate, dissolution time, and tapped density. Antioxidant activity was quantified using the DPPH (2,2-diphenyl-1-picrylhydrazyl) assay, reporting IC_{50} values. All instant granule formulations successfully met the established physical quality requirements across all evaluated parameters. Furthermore, the antioxidant activity demonstrated a concentration-dependent effect, with IC_{50} values of 119.576 ppm for Formula 1, 82.000 ppm for Formula 2, and 59.962 ppm for Formula 3. This study confirms that instant granules formulated with a single black *A. sativum* extract exhibit significant antioxidant potential and possess desirable physical characteristics, indicating their promise as a natural antioxidant supplement.

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INTRODUCTION

Health supplements are gaining increasing recognition as products designed to augment nutritional intake and support, enhance, or sustain various physiological functions. These supplements are available in diverse dosage forms, including powders, which are characterized by their homogeneous, finely granulated nature, making them suitable for convenient consumption[1]. A promising source for such beneficial natural products is single garlic (*Allium sativum* L.), a well-regarded botanical with a long history of use[2].

Among the various forms of *A. sativum*, black *A. sativum* stands out as a unique product derived from the controlled fermentation of single *A. sativum*. This process typically involves prolonged exposure to high temperatures (60-90°C) and humidity (70-80%) for a month or more[3]. The fermentation induces a series of non-enzymatic reactions, leading to distinct changes in the *A. sativum*'s characteristics: its color transforms to black, a sweet taste develops, and its texture becomes notably chewy and jelly-like[4].

Crucially, the fermentation process enhances the bioactivity of *A. sativum*. Studies have shown a significant increase in the active compound content of black *A. sativum* compared to raw *A. sativum*. For instance, the polyphenol content in black *A.*

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sativum skins can increase six-fold, and both total polyphenol and flavonoid levels are substantially elevated during the heating process[5]. Consequently, black *A. sativum* exhibits more potent antioxidant activity in both *in vitro* and *in vivo* models than its raw counterpart[4,6].

Despite its enhanced beneficial properties, the application of black *A. sativum* in instant granule formulations remains largely unexplored. Developing black *A. sativum* into granules offers several advantages, including improved physical and chemical stability, enhanced flow characteristics, and greater ease of preparation for consumption. Prior research, such as that by Putri *et al.*[7] on Dayak onions, has successfully demonstrated the development of instant granules with favorable antioxidant properties and physical characteristics. Building upon this foundation, the present study aims to formulate an instant granule powder from a 70% ethanol extract of single *A. sativum* and comprehensively evaluate its antioxidant effect, alongside a thorough physical characterization of the prepared powder.

MATERIALS AND METHODS

Materials

All chemical reagents utilized in this study were of analytical grade, ensuring high purity and reliability for experimental procedures. The excipients employed in the instant granule formulation included stevia powder, polyvinylpyrrolidone (PVP) K30, 96% ethanol, sodium carboxymethyl cellulose (Na-CMC), mannitol, and lactose. The primary material utilized in this research was a single black *A. sativum* sourced from Lumajang, East Java, Indonesia. Plant identification and authentication were rigorously performed by the Herbarium Bogoriense, Botany Division, Biology Research and Development Center-BRIN Cibinong, Indonesia, with certificate number 301/IPH.1.01./If.07/II/2019.

Methods

Extraction

Allium sativum bulbs were weighed and subsequently subjected to controlled fermentation within a climate chamber maintained at an optimal temperature of 70°C and 90% humidity for a period of 30 days[8]. Following this fermentation process, the resulting black *A. sativum* was retrieved and aerated according to the specific fermentation duration. For extraction, the maceration method was employed, utilizing a 1:2 ratio of black *A. sativum* to 70% ethanol. The crude extract was then frozen at -80°C and subjected to lyophilization using a freeze dryer. The prepared black *A. sativum* extract underwent comprehensive analysis for its organoleptic profile, extract yield, ash content, water content, and residual solvent presence to ensure quality and consistency.

Phytochemical screening

Phytochemical screening was systematically conducted to identify the presence of key secondary metabolite compounds within the single black *A. sativum* extract. This comprehensive analysis specifically targeted the qualitative detection of alkaloids, flavonoids, tannins, saponins, and steroids/triterpenoids, providing insights into the extract's chemical composition[9].

Formulation of instant granules

The instant granule formulation, adapted from Putri *et al.*[7], with slight modifications, is detailed in **Table I**. This formulation for a single black *A. sativum* extract was based on established solid formulation principles. Initially, a black *A. sativum* extract preparation was made to a predetermined concentration. Lactose was then gradually incorporated into the single black *A. sativum* extract, followed by the sequential addition of mannitol, Na-CMC, and stevia powder. These components were thoroughly mixed until a homogeneous blend was achieved. Subsequently, a PVP binder solution was added dropwise to this mixture, with continuous mixing, until a cohesive, compressible mass formed. This mass was then passed through a No. 12 sieve. The resulting sieved material was evenly spread on a shallow tray and dried at 50°C for 24 hours. Following drying, the granules were re-sieved using a No. 14 sieve to ensure uniform particle size. The formed granules were then subjected to various physical characteristic tests to assess their quality.

Table I. Formulation of single black *A. sativum* extract instant granules.

Ingredients	Function	Amount (%)		
		F1	F2	F3
Single black *A. sativum* extract	Active	5	7.5	10
PVP K30	Binder	0.5	0.5	0.5
Na-CMC	Dispersing	0.25	0.25	025
Stevia	Sweetener	1	1	1
Mannitol	Filler	25	25	25
Lactose	Filler	Ad 100	Ad 100	Ad 100

Physical evaluation of instant granules

The physical evaluation of the instant granules formulated from a single black *A. sativum* extract commenced with a comprehensive set of tests. These assessments included an organoleptic analysis to evaluate sensory attributes, determination of moisture content, measurement of flow rate and angle of repose to ascertain powder flow properties, and assessment of tapped density to understand packing characteristics. Finally, the dissolution time of the granules was measured to evaluate their disintegration and release profile[10].

Antioxidant activity test

The antioxidant activity of the instant granules was assessed using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay, a method adapted from Fidrianny *et al*[11]. This spectrophotometric technique quantifies the reduction of DPPH radicals by antioxidant compounds, with absorbance measured at a wavelength of 516 nm. In this study, ascorbic acid was utilized as the positive standard for comparison. The percentage of DPPH radical scavenging activity, or inhibition, was calculated using the following **Equation 1**:

$$\%\text{inhibition} = \frac{\text{DPPH absorbance} - \text{Sample absorbance}}{\text{DPPH absorbance}} \times 100\% \qquad [1]$$

Data analysis

Statistical analysis for this research was performed using SPSS version 25. To determine statistically significant differences, a p-value of <0.05 was established as the threshold.

RESULTS AND DISCUSSION

During the fermentation process, significant organoleptic changes were observed in the *A. sativum* samples, with a noticeable browning and alteration in taste beginning around day 17. This transformation is attributed to the Maillard reaction, a well-documented non-enzymatic browning process that occurs between reducing sugars and amino acids. As fermentation progresses, this reaction yields complex, high-molecular-weight compounds known as melanoidins, which are responsible for the characteristic dark brown or black color of the final product[12]. Furthermore, the Maillard reaction not only influences color but also generates a variety of volatile compounds, which contribute to the development of a milder aroma and a distinctly sweeter[13], less pungent taste in the fermented *A. sativum*.

The ethanolic extraction of single black *A. sativum* yielded a semisolid, brown extract (**Figure 1**) with a distinct characteristic aroma, achieving a yield of 15%. Further characterization revealed a water content of 1.58%, which falls well within the acceptable quality standard of ≤10%[11]. This low water content is crucial for maintaining the long-term stability and durability of the extract during storage[14]. The ash content, determined to be 2.10%, also conformed to the established standard of ≤16.6%[11], providing an indication of the mineral content derived from the raw material and the efficiency of the extraction process. Critically, the residual solvent content of the extract was found to be 0.39%, comfortably meeting the stringent requirement of not exceeding 1% for traditional medicinal ingredients[15].

The phytochemical screening results, presented in **Table II**, indicate the presence of several key secondary metabolites in the extract. Specifically, flavonoids, saponins, and tannins were detected, suggesting their contribution to the observed biological activities. Conversely, alkaloids and steroids/triterpenoids were not identified in the sample. This particular phytochemical profile aligns with previous studies on single black *A. sativum*, which often highlight the abundance of phenolic compounds and saponins known for their diverse pharmacological properties[16,17].

a **b** **c**

Figure 1. Single black *A. sativum* instant granules. (**a**) F1, (**b**) F2, and (**c**) F3.

Table II. Phytochemical screening of single black *A. sativum* extract instant granules.

Compounds	Results
Alkaloids	Negative
Flavonoids	Positive
Saponins	Positive
Tannins	Positive
Steroids/Triterpenoids	Negative

The organoleptic assessment, a critical parameter for ensuring product consistency and consumer acceptance, involved the direct observation of the granules' color, taste, and aroma[18]. In this study, three distinct formulations of single black *A. sativum* extract instant granules (F1, F2, and F3) were developed and evaluated. All three formulations consistently exhibited a fine granular powder form and retained the characteristic pungent aroma of single black *A. sativum*. While F1 and F2 presented a consistent white color, F3 displayed a light brown hue. Despite this slight color variation, the overall appearance and characteristic aroma were largely uniform across all three formulations. Furthermore, a consistent sweet taste was noted in each of the developed formulas. These findings collectively indicate that the instant granule preparations of F1, F2, and F3 possess remarkably similar physical characteristics, suggesting a robust and reproducible manufacturing process.

The moisture content of the prepared instant granules was assessed using a moisture analyzer, a crucial parameter influencing granule quality and stability[19]. An ideal moisture content for pharmaceutical granules typically falls within the range of 1-5%[20]. Our analysis revealed that all three formulated instant granule batches satisfied this critical requirement. Specifically, F1 exhibited a moisture content of 2.03%, F2 was 1.83%, and F3 measured 1.3% (**Table III**). These results, consistently ranging between 1% and 2%, are well within the acceptable limits for good quality granules, demonstrating effective drying and formulation processes. The low moisture content is vital for preventing microbial growth, maintaining product stability, and ensuring optimal flowability and compressibility during subsequent processing or patient administration[21].

Table III. Moisture content of single black *A. sativum* extract instant granules.

Formulas	Moisture content (%)
F1	2.03
F2	1.83
F3	1.30

The results of the granule flow rate test demonstrate that all three developed formulations (F1, F2, and F3) met the established requirements for flow speed. Specifically, F1 exhibited an average granule flow speed of 8.10 ± 0.31 seconds, F2 measured 7.46 ± 0.38 seconds, and F3 recorded the fastest flow time at 5.29 ± 0.42 seconds (**Table IV**). The superior flowability observed in F3 is likely attributable to its lower water content, which consequently reduces inter-particulate frictional forces, thereby facilitating faster granule flow. According to established pharmaceutical standards, an ideal flow time for 25 g of granules ranges from 4 to 10 seconds[22], indicating that all three formulations possess good flow properties, crucial for efficient tablet compression or capsule filling.

Table IV. Flow rate of single black *A. sativum* extract instant granules.

Formulas	Flow rate (seconds)
F1	8.10 ± 0.31
F2	7.46 ± 0.38
F3	5.29 ± 0.42

The angle of repose test is a crucial measure of powder flowability, defined as the constant angle formed between the cone of a granular material and the horizontal plane. A well-established criterion for good flow properties specifies an angle of repose ranging from 25° to 40°[23]. In the present study, all three formulated granule batches met these established requirements, as detailed in **Table V**. Specifically, the average angle of repose for F1 was 32.45°, for F2 it was 30.07°, and for F3 it was 28.28°. These values fall within the acceptable range of 25° < α < 40°[24], indicating satisfactory flow characteristics for all formulations.

Table V. The angle of repose of single black *A. sativum* extracts instant granules.

Formulas	The angle of repose (°)
F1	32.45
F2	30.07
F3	28.28

Several intrinsic properties of granules, including shape, size, and instantaneous moisture content, are known to influence the angle of repose[23]. While our formulations demonstrated acceptable flow, it is important to note that heterogeneity in granule size can negatively impact the angle of repose, potentially leading to poorer flow properties. Furthermore, a direct correlation exists between the angle of repose and flow time: optimal flow time typically corresponds to a desirable angle of repose, whereas suboptimal flow time often indicates an unfavorable angle of repose[24].

The tapped density analysis of the prepared granules demonstrated that all three formulations (F1, F2, and F3) met established quality requirements. Specifically, the average tapped density values were 0.561 g/mL for F1, 0.555 g/mL for F2, and 0.592 g/mL for F3 (**Table VI**). These values fall within the acceptable range of 0.2 – 0.6 g/mL for good tapped density[25]. The observed variations in tapped density among the formulas are likely attributable to subtle differences in granule particle size, which consequently influence the inter-particulate void spaces[26]. Furthermore, the compressibility percentage, indicative of the reduction in granule volume due to tapping and vibration, was evaluated. The tapping trial results showed compressibility percentages of 11% for F1, 10% for F2, and 5.6% for F3. All three formulations exhibited excellent compressibility, as values below 20% are generally indicative of good flow properties for powders or granules[27].

Table VI. Tapped density and compressibility of single black *A. sativum* extracts instant granules.

Formulas	Tapped density (g/mL)	Compressibility (%)
F1	0.561	11
F2	0.555	10
F3	0.592	5.6

The dissolution time of the developed granules was assessed by adding 10 g of granules to 100 mL of deionized water, followed by stirring at 500 rpm with a magnetic stirrer. The time required for complete dissolution of the granules was recorded. A dissolution time of less than 5 minutes was considered to meet the established standard requirement[25]. Results from the dissolution time test indicated that all three formulated granule batches met this requirement. Specifically, the average dissolution time for F1 granules was 0.49 minutes, for F2 it was 2.03 minutes, and for F3 it was 2.31 minutes (**Table VII**).

Table VII. The dissolution time of single black *A. sativum* extracts instant granules.

Formulas	Dissolution time (minutes)
F1	0.49
F2	2.03
F3	2.31

The antioxidant activity of the black *A. sativum* extract was initially confirmed, establishing its inherent radical scavenging capabilities. Subsequently, the antioxidant efficacy of the instant granule formulations was evaluated at varying

concentrations of black *A. sativum* extract: 5% (F1), 7.5% (F2), and 10% (F3). As hypothesized, a direct correlation was observed between increasing extract concentration within the formulations and an enhanced inhibition percentage, indicative of stronger antioxidant potential. Specifically, the IC_{50} value for F1 (5% extract) was determined to be 119.576 µg/mL. This activity significantly improved with higher concentrations, with F2 (7.5% extract) achieving an IC_{50} of 82.000 µg/mL and F3 (10% extract) demonstrating the strongest activity at an IC_{50} of 59.962 µg/mL (**Table VIII**). These IC_{50} values classify all three formulations as possessing moderate to strong antioxidant activity, falling within the range of 50-150 µg/mL[28]. This concentration-dependent enhancement in antioxidant capacity is likely attributable to the presence of potent antioxidant compounds inherent in black *A. sativum* extract, particularly polyphenols and flavonoids. For comparative purposes, ascorbic acid was utilized as a positive control, yielding an IC_{50} of 13.360 µg/mL.

Table VIII. The antioxidant activity of single black *A. sativum* extracts instant granules.

Formulas	IC_{50} (µg/mL)
F1	119.576
F2	82.000
F3	59.962
Ascorbic acid	13.360

CONCLUSION

In this study, we successfully formulated instant antioxidant granules utilizing a 70% ethanol extract of single black *A. sativum*. Three concentrations were investigated: F1 (5%), F2 (7.5%), and F3 (10%). All developed formulations demonstrated favorable physical properties, indicating their suitability as a solid dosage form. Furthermore, the instant granules exhibited moderate to strong antioxidant activities, with the highest potency observed in formulation F3. Specifically, F3 achieved an IC_{50} value of 59.962 ppm, highlighting its robust antioxidant capacity.

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AUTHORS' CONTRIBUTION

Conceptualization: Abdul Aziz Setiawan
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Visualization: -
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DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this study.

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