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# Formulation of Effervescent Powder Using Dates Containing Myo-Inositol as Active Ingredients

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**Abstract**

The objective of this research is to explore the impact of incorporating effervescent powder as a medium to synergize the potential health benefits of myo-inositol with the inherent sweetness of dates. The first step in the study was to use the HPLC method to determine the myo-inositol compound in dates. Next, five formulations were prepared from myo-inositol, dates and effervescent base which generated form mixture design software in different concentrations. Making effervescent powder began with weighing all the ingredients according to the formulation. The prepared effervescent powder was evaluated for dissolution time, water solubility, pH testing and antioxidant activity. According to the findings, the effervescent powder's pH is between 4.05 to 5.02 which between the range for intended used. In addition, the effervescent powder dissolves in a short amount of time between 103 and 135 seconds. Testing for water solubility shows results between 1:24 and 2:26 minutes, with little difference between the different formulations. Lastly, formulation 1, which contains myo-inositol and the effervescent agent, has the highest percentage of inhibition in the DPPH testing which at the value of 49.75 ±1.19. For the rest of the formulation which consist of the mixture of dates, myo-inositol and effervescent agent, resulted constant percentage inhibition for DPPH assay in the range of 39.72 ±2.08% until 42.72 ±6.72%. This study reveals the fascinating potential of utilising dates and myo-inositol together in an effervescent powder, providing a new way of utilising each ingredient's benefits for sweetness and health.

## 1. Introduction

Effervescent powders have become popular due to their convenience, quick dissolving nature, and easy administration [1]. Creating effective effervescent powders requires careful selection of active ingredients and additives to achieve desired therapeutic effects. Recently, there's been interest in using natural substances in pharmaceutical formulations for potential health benefits. Dates, known for their rich nutrients and natural sweetness, have gained attention as a potential natural ingredient in various food and wellness products [2]. They contain myo-inositol, a bioactive compound that has possible research for its potential medicinal advantages.

Myo-inositol is a molecule found in many living organisms and belongs to the B vitamin family. It is synthesized in large amounts by the body from D-glucose. Myo-inositol is considered safe and has shown promise in addressing fertility and pregnancy-related issues. It can normalize ovarian function and improve oocyte and embryo quality in PCOS. Foods like grains, maize, meat, citrus fruits, and legumes contain myo-

inositol, and it is also available as a dietary supplement [3]. It plays a crucial role in various human processes, including the regulation of glucose metabolism [27].

The combination of myo-inositol and dates in effervescent powder could enhance the potential health benefits of the drink. Additionally, the addition of myo-inositol aims to improve the effervescent powder's properties, making it more appealing and effective. High-performance liquid chromatography (HPLC), a reliable analytical technique [30], can accurately measure myo-inositol in dates. This method is particularly useful for determining myo-inositol content in dates powder, offering valuable insights into its concentration. In summary, the use of HPLC in this study allows for a comprehensive evaluation of dates powder as a natural sweetener, with a focus on its active component, myo-inositol. Assessing the antioxidant activity of dates powder helps determine its potential health benefits.

However, dates' nutritional content and myo-inositol levels are studied, incorporating them into effervescent powders is largely unexplored. To create such a powder, the need to define myo-inositol concentration, assess its compatibility with other substances, and evaluate the powder's physicochemical properties. This study attempts to formulate effervescent powder using dates enriched with myo-inositol and to determine the antioxidant properties of the final effervescent powder.

## 2. Materials and Method

### 2.1 Raw materials

The main ingredients used in this study were powdered dates and myo-inositol, which were both purchased from local store located at Penang. The brand that produced the myo-inositol used in the study, Take It Global Sdn Bhd. Furthermore, A&T Ingredients, a different Penang-based firm, provided the dates powder used in the study. Those are the base ingredients for the effervescent powder composition. They also had a thorough analysis using High-Performance Liquid Chromatography (HPLC) to accurately identify the myo-inositol compound. To verify the existence of myo-inositol in the dates, this analysis included the retention time seen in the HPLC data.

Citric acid was used in this study for the acidic element on having the effervescent production. Because of its great solubility, sour taste, and capacity to promote effervescence, citric acid is a common acid ingredient in effervescent powder formulations [8]. For instance, one study uses citric acid concentrations between 7.35% and 8.08%. This shows the range of previously studied citric acid concentrations and be used as a guide for the formulation in this study [5]. Specific uses of sodium bicarbonate in effervescent compositions are highlighted in some patent applications. An effervescent formulation comprising 5.25% sodium bicarbonate [4], for instance, it was disclosed in one patent application.

### 2.2 Screening myo-inositol compound in dates by using HPLC

HPLC analysis was conducted using an LC-10A UFLC system, featuring a SIL-HT automatic sample injector from Shimadzu in Kyoto, Japan, and a UV/VIS detector (SPD-M20A) paired with a C18 reversed-phase column (250 mm × 4.6 mm, 5 µm, Milford, MA). The mobile phase method modified from [7] consisted of deionized water as phase A and a mixture of 5% formic acid in 95% HPLC-grade methanol as phase B, with a ratio of 5:95, equivalent to 1 liter. Detection was performed at 546 nm, with a 10 µL sample eluted through the system over a 25-minute period according to [9], at a flow rate of 1.0 ml/min and a column temperature set at 40 °C [7]. For sample preparation, the necessary equipment included a 0.45 µm membrane filter, test tubes, sample vials, and syringes. The standard preparation involved a five-fold sample dilution procedure. The standard formula was used for the standard curve dilution. The equations for deriving standard solutions are M1V1 = M2V2.

### 2.3 Effervescent powder making

Effervescent agent which are citric acid and sodium bicarbonate are purchased from a local food additive supplier were selected as constant variables, whereas the effervescent powder formulation measured were antioxidant level, pH, disintegration time and water solubility. To observe the effect of ingredients on the physicochemical analysis of the effervescent powder, experiments were systematically conducted by using Simplex Lattice Mixture Design (Trial Version 14) software. The formulation of effervescent powder was prepared as shown in Table 1. The myo-inositol, dates powder with the effervescent agent was weighed and mixed for further used.

**Table 1** *Formulation of Effervescent Powder by using Mixture Design*

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| Ingredients | Formulation (mg) | | | | |
|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 |
| **Myo-inositol** | 1270 | 0 | 635 | 317.5 | 952.5 |
| **Dates** | 0 | 1270 | 635 | 952.5 | 317.5 |
| **Citric Acid** | 425 | 425 | 425 | 425 | 425 |
| **Sodium Bicarbonate** | 305 | 305 | 305 | 305 | 305 |

## 2.4 Antioxidant Activity

Using a few modifications from, the [10] was applied to measure the antioxidant activity. An antioxidant assay based on electron transfer the DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) free radical approach yields a violet solution in methanol. The percentage of antioxidant activity (AA%) for each chemical is the anticipated outcome for antioxidant activity when using the DPPH technique. The instrument used to undergo DPPH analysis was using UV-Vis spectrophotometer (T60 UV-VIS Spectrophotometer). First, a 0.1 mM DPPH solution was prepared by dissolving 0.0039 g of DPPH reagent in 100 mL of 99.5% methanol. For the preparation of effervescent powder samples (the total samples were 5 samples) were prepared. Because the samples are all in powder form. All the samples undergo extraction process with medication method from [26], where the sample are weighed accurately 1g and diluted with 10 ml of deionized water and 10 ml of 99.5% methanol then, all the samples are placed in a water bath for one hour at 35°C. In each test tube, 800 µL of brewed sample were mixed immediately with 1200 µL of methanol. Subsequently, 4000 µL of the 0.1mM DPPH solution were added, and the mixture was kept in darkness for 30 minutes. The degree of discolouration, expressed as a percentage of inhibition, reveals the antioxidant compound's capacity for scavenging. The absorbance was determined at $\lambda$ = 517 nm using a Spectra max 340 microplate reader. Equation 1 was used to calculate the percentage inhibition value [23]. % of antioxidant activity= [(Ac−As) ÷Ac] × 100. Where Ac indicate to control reaction absorbance and As is testing specimen absorbance.

## 2.5 pH Testing

Using a pH meter, (EUTECH Instrumentals, Singapore) the samples are dissolved in water, the effervescent powder's pH were determined. Weighing out and dissolving about 2g of powder in 50 ml of water is a modified procedure based on research done by [24]. A pH meter was used to ascertain the pH of the solution once the granules have fully dissolved. To ensure precision, this procedure will be carried out three times utilizing triplicate measurements.

## 2.6 Dissolution Time

The dissolution time method was conducted by the amount of time needed for the powder to completely fizzy where the carbonation formation happens then the time taken will be calculate by using a stopwatch (Anes Thabit *et al.,* 2018). The sample was weighed for 2 g of the powder in a beaker diluted with 50 mL of water. For every treatment to achieve the required dissolved time, a good effervescent dispersion time, according to [19], is less than five minutes since if it is longer, the effervescent quality would be reduced. According to [14] calculating the dissolution time using a stopwatch starting from the tablet immersed until all the tablets disintegrated and dissolved. The duration needed for a powder to fully dissolved was assessed through visual examination [28].

## 2.7 Water Solubility

Solubility testing was measured by using beaker method which by taking effervescent powder and place it in a 100ml beaker (with 50ml of water at a temperature of 20°C±5°C), that is, many bubbles are released. When the gas around the powder or fragments stops escaping, the powder should dissolve or disperse in water, and no aggregated particles remain [1]. Then, right after the powder are fully dissolved, the time taken will be recorded.

## 2.8 Statistical Analysis

The experimental data for the study was analysed using analysis of variance (ANOVA) in a completely random design. The level of significance for the statistical analysis was established at $p \leq 0.05$, and Tukey's test was used to determine the distinction between means [6]. Analysis of variance (ANOVA) was used to examine the experiment's data and identify the main impacts and interrelationships of the variables.

## 3. Result and Discussion

The results are achieved for qualitative analysis on determining the myo-inositol compound in dates by using HPLC. The effervescent powder undergoes few chemical analyses which are typically tested for effervescent formulation. Each analysis had been analyzed statistically to shows its significance difference.

### 3.1 Observation of myo-inositol compound in dates by using HPLC

A major source of carbohydrates in some diets is myo-inositol, a cyclic carbohydrate with six hydroxyl groups that is present in a variety of food sources. As a result of their many hydroxy groups, carbohydrates are recognised to be non-volatile and thermally liable substances [32] In this experiment, HPLC is used to identify the present of myo-inositol in dates sample. Although gas chromatography (GC) has a higher sensitivity and speed, it cannot be utilised in this case as the compound are not sufficiently volatile. The response is displayed on a graph where the x-axis is the retention time, and the y-axis is a measure of the intensity of the response. In the myo-inositol standard chromatogram, two distinct peaks were observed. The first peak, occurring at a retention time of 1.982 minutes, exhibited an area of 2,645 $cm^2$ and a height of 28,763 cm. Moving to the second peak, identified at a retention time of 2.215 minutes, it displayed an area of 102,523 $cm^2$ and a height of 17,327 cm. These measurements were recorded for the myo-inositol standard at a concentration dilution of 10^4. An HPLC chromatogram's total height and total area of a peak indicate the signal's intensity and can be used to calculate how much of the compound is in the sample with the respective retention time and concentration [31]. In the study by [32] the peak first peak was identified with a 41232µ peak area after 4.8 minutes, whereas the second peak was identified with a 41341µ peak area after 4.7 minutes. When compared to the standard myo-inositol from the previous study, the peak graph obtained may not be true due to the early presence of the elution component.

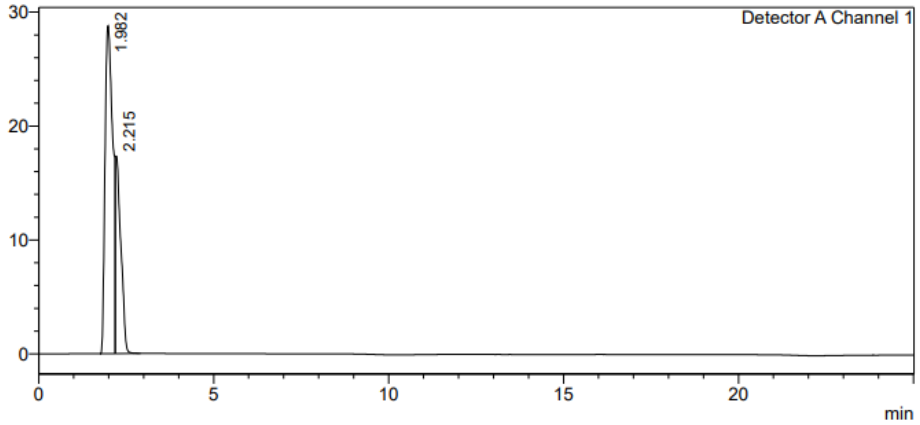


**Fig. 1** *HPLC Chromatogram of myo-inositol sample.*

Fig. 2 show the peak area on dates chromatogram sample which result quite not far compared to the retention time of myo-inositol standard at dilution 10^4. From Fig. 2 shows at peak 1 at the area of 2645 $cm^2$ indicates the retention time at 1.786. While for the second peak, at the area of 640197 $cm^2$ with the height at 32490 cm showed the retention time 2.015 minutes. As compared to the retention time from the standard, possibility of the compound present in the dates might be there but due to the handling error while constructing the experiment might affect the result of the peak area. Moreover, the elution separation might be affected.

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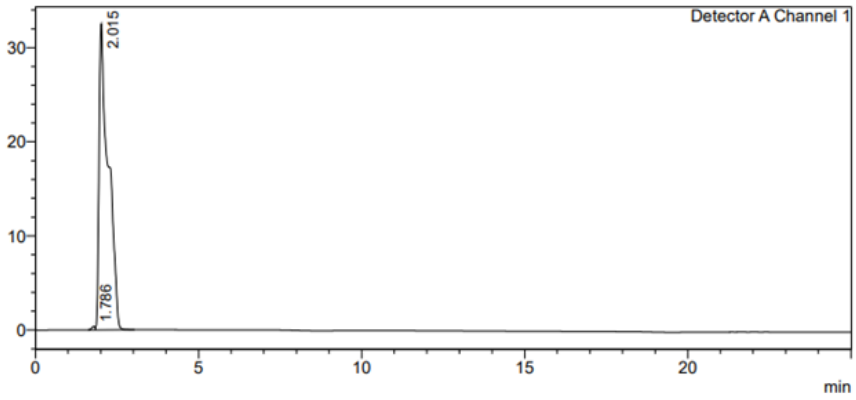


**Fig. 2** *HPLC Chromatogram of dates sample*

Before chromatographic analysis of the sample, calibration is done to establish a relationship between signals, or the response detected and the concentration of the analyte. External calibration, which was the one used in the experiment, involves the construction of a standard curve by injecting different concentrations of a known standard and interpolating from there the concentration of subsequent runs. Fig. 3 is the peak area vs Concentration to construct a standard curve for myo-inositol standard.

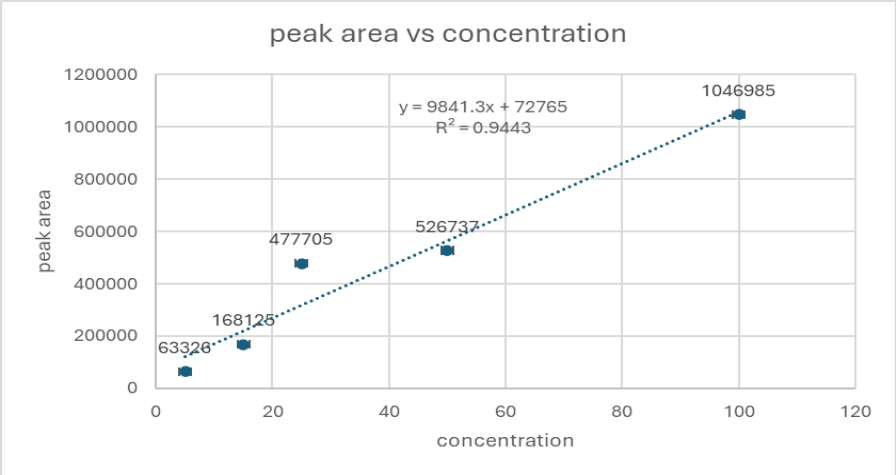


**Fig. 3** *Standard curve obtained from myo-inositol standard*

The possibility of the compound present in the dates might be there but due to the handling error while constructing the experiment might affect the result of the peak area. Moreover, the elution separation might be affected. Calibration is done to create a link between the detected signals or responses before chromatographic analysis of the material is carried out. The experiment used different concentrations of a known standard onto a standard curve and used that curve to estimate the concentration of following runs. Hence, concentration of 7.097 mg/L it shows the presence of myo-inositol in dates sample. However, the peak hasn't shown a good peak separation. The results obtained was not accurate since all the point are not met with the straight line where it does affect the value of R2 where the value is 0.94493. The column's homogeneous C18 coating could possibly be one the factor of the inefficiency.

## 3.2 Physicochemical Analysis

The effervescent powder is tested to ensure that it is appropriate for the stated claims, and physicochemical analysis is an essential part of that testing. This analysis includes evaluating the pH, determining the dissolution time, determining the solubility in water, and lastly looking at the antioxidant activity.

**Table 2** *Chemical analysis of effervescent powder of dates containing myo-inositol*

| Property | Formulation | | | | |
|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 |
| **Ph testing** | 5.07 ± 0.55[a] | 5.12 ± 0.42[a] | 4.78 ± 0.21[a] | 4.71 ± 0.32[a] | 4.50 ± 0.49[a] |
| **Dissolution time** | 1.89 ± 0.27[a] | 2.49 ± 0.01[a] | 1.99 ±0.34[a] | 2.15 ±0.04[a] | 1.88 ±0.25[a] |
| **Water solubility** | 2.26 ± 0.19[a] | 1.74 ±0.31[a] | 1.24 ±0.20[a] | 1.58 ±0.46[a] | 1.52 ±0.47[a] |
| **Antioxidant activity** | 49.75 ±1.19[a] | 42.72 ±6.72[b] | 40.02 ±3.00[ab] | 39.72 ±2.08[ab] | 41.90±5.28[ab] |

### 3.2.1 pH Testing

Effervescent powder undergoes triplicate measurements to assess the pH levels, and it was resulted that the recorded pH values exhibited minimal variation among the replicates. The pH readings obtained in this analysis ranged between 4.05 and 5.02. This range is considered suitable for effervescent drinks, as it indicates a mildly acidic to neutral pH level, which is generally well-tolerated by the body and is in line with the pH values of other effervescent products such as tablets containing vitamin C. The chemical compound from the variables ingredients in the powder can barely affected the pH of the effervescent solution [20]. The chemical compound from the variables ingredients in the powder can barely affect the pH of the effervescent solution [22]. However, it was still acceptable as the pH value was less than 6 could improve the absorption of effervescent tablets [1].

### 3.2.2 Dissolution Time

Effervescent powder had a dissolution time less than three minutes, namely 103-135 seconds. So that all treatments met the standard dissolved time. In addition, the results show no significant different between all the formulations due to the constant weight of effervescent agent in every formulation. This test is crucial for assessing the performance and quality of effervescent tablets and powders. It helps ensure that the product dissolves within a specified time frame, which is important for its effectiveness and bioavailability. A higher moisture content can lead to faster dissolution in water, while a lower moisture content can result in a slower dissolution rate [14]. According to [19], good effervescent dispersion time is less than 5 minutes because if more than the effervescent quality is not good. Sodium bicarbonate will produce a relatively shorter dissolution time because sodium bicarbonate is a crushing agent when reacting with acid. The addition of sodium bicarbonate and citric acid with a balanced ratio results in the fastest dissolution time [12].

### 3.2.3 Water solubility

The water solubility test results are all in a range between 1:24 until 2:26 minutes which equivalent to 146 seconds. The result was statistically tasted shows no significant difference between all formulation. Besides, due to the effervescent agent weight in each formulation is consistent, the data do not indicate any substantial differences between any of the formulations. Effervescent tablets granules are designed to be dissolved or dispersed in water before administration, and the solubility of the effervescent powder is crucial for their effectiveness [27]. The end product's taste, effectiveness, and user experience are all strongly impacted by how soluble effervescent granules are in water [1]. Each ingredient contributes to the water solubility test. Myo-inositol has the highest solubility in water making it a suitable good solvent [14]. Myo-inositol powder is highly soluble in water, dissolving immediately in room temperature water and taking slightly longer in cold water. The solubility of myo-inositol in water is also supported by its chemical properties, as it is classified as a water-soluble compound [29]. The solubility of date powder exceeded 80%, making it a versatile ingredient suitable for blending with various food products [13]. Citric acid has high fluidity, followed by sodium bicarbonate [15]. The acidic component responsible for the effervescent generation was citric acid. Citric acid is a common acid ingredient in effervescent powder formulations due to its excellent solubility, sour taste, and ability to enhance effervescence [8] According to study by, [11] sodium bicarbonate is an essential component that improves the solubility of effervescent tablets.

### 3.2.4 Antioxidant activity

The antioxidant activity was represented as DPPH radical scavenging activity (RSA), a metric that quantifies the antioxidant capacity of a sample and is determined by the percentage of DPPH radicals neutralized by the sample. A sample with a higher RSA value has a higher capacity to scavenge DPPH radicals, indicating a stronger antioxidant activity. In other words, a greater proportion of neutralized DPPH radicals indicates a stronger antioxidant effect. By referring to Table 2 for formulation 1 and 2 the infusion inhibited DPPH absorption are 49.75±1.19% and 42.72±6.72% respectively. Formulation 3, 4 and 5 shows inhibition activity 41.02±3.00%, 39.72±2.08%, 41.90±5.28% respectively which is significantly lower than formulation 1 and 2. Those three

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results are at constant rate for percentage inhibition of DPPH absorption which indicate moderate level of inhibition DPPH absorption.

The constant percentage inhibition observed in the combined effervescent drink formulation shows a consistent effect. However, it is important to note that dates, rich in sugars like fructose, can undergo glycation, potentially contributing to antioxidant activity. Yet, this process may also compete with myo-inositol in scavenging DPPH radicals, potentially lowering the measured inhibition of myo-inositol.

Citric acid is one of the secondary antioxidants that are frequently added to create a combination with primary antioxidants, if considering at the other ingredients in the formulation. The synergistic effect of this combination will increase the efficacy of primary antioxidants' work. Since citric acid compounds to bind metals that oxidize polyphenolic compounds, there is an additive interaction between citric acid and polyphenols [11]. In conclusion, the combination of two variables on the formulation which is myo-inositol and dates gives a moderate percentage of inhibition which proven the antioxidant activity present in the formulation. In conclusion, the combination of two variables on the formulation which is myo-inositol and dates gives a moderate percentage of inhibition which proven the antioxidant activity present in the formulation.

Next, the comparison absorption inhibition of DPPH towards one effervescent powder formulation and control sample which are myo-inositol and 1g of dates which indicate antioxidant properties for each sample. Myo-inositol have the highest inhibited DPPH absorption which by 47.75%. Next, 1 gram of dates sample shows inhibition activity of 43.72% which is significantly higher than effervescent powder sample and slightly lower than myo-inositol sample. The dates sample shows lower inhibition percentage compared to myo-inositol sample possibly due to the level treatments of the dates fruit to become a fine powder. According to [21] food processing and handling methods such as thermal processing can also deplete the natural antioxidants in foods, leading to a decrease in the antioxidant level. Fig. 4 shows the result for comparison between sample formulation, commercial myo-inositol sample, and dates powder.

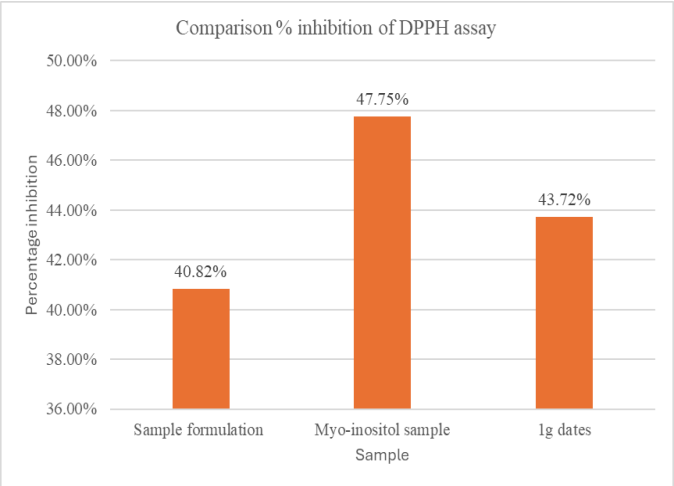


**Fig. 4** *Graph bar shows DPPH assay for comparison between sample formulation, commercial myo-inositol sample and 1g dates sample expressed in percentage inhibition*

Since the percentage of dates powder are lower than commercial myo-inositol sample it is possible due to some interference from other chemical reactions. Glycation in dates involves the chemical reaction between natural sugars, primarily fructose, and amino acids, forming Advanced Glycation End products (AGEs) over time, especially in warm or humid conditions. Additionally, the interference in DPPH scavenging could be influenced by other factors, including bioactive components in dates associated with antioxidant capacity in various studies [20] [16]. Different date varieties have shown 55-75% antioxidant capacity [17], and dates are rich in phytochemicals like carotenoids and phenolic compounds that enhance antioxidant properties. Variations in date variety, growth stage, and geographical factors can affect phenolic compounds, potentially impacting antioxidant content. The use of dates at various ripeness levels [18] and also the type of dates powder processing technique may have influenced their ability to scavenge DPPH radicals, with other compounds like myo-inositol possibly competing in the scavenging process, potentially affecting DPPH test outcomes.

## 4. Conclusion

Initial analysis detected myo-inositol in the samples calculated from standard curve with a concentration of 7.097 mg/L indicated the presence of myo-inositol in the samples, providing an essential foundation for the

subsequent investigations. However, the imprecise results, reflected in a non-ideal R2 value of 0.94493, indicated potential errors in solution preparation. This prompted a closer examination of experimental procedures. Physicochemical analysis of the effervescent powder included pH tests, dissolution time assessment, water solubility evaluation, and antioxidant activity testing. pH tests confirmed that all formulations fell within the desired range (pH 4.05 to 5.02) for the effervescent drink, indicating suitability for use. Dissolution time analysis demonstrated that the powder dissolved in under three minutes, meeting quality standards. The water solubility test shows no significant difference between all formulations which are all in a range between 1:24 until 2:26 minutes. The results of water solubility evaluation are all influence by every ingredient in the effervescent powder. Lastly, formulation 1, which contains myo-inositol and the effervescent agent, has the highest percentage of inhibition in the DPPH testing which at the value of 49.75 ±1.19. The DPPH assay indicated a moderate level of antioxidants in the effervescent powder, suggesting reasonable but not exceptionally high antioxidant activity. While not offering the highest level of protection, these formulations still hold potential for health benefits. To summarise, formulation 1 reveals a greater percentage inhibition in DPPH testing, whereas all other formulations show no significant differences across physicochemical analyses, but the results still fall within the range of accepted effervescent use.

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## Conflict of Interest

Authors declare that there is no conflict of interests regarding the publication of the paper.

## Author Contribution

*The authors confirm contribution to the paper as follows:* ***study conception and design:*** *Nur Naufal binti Aznan, Siti Fatimah Zaharah binti Mohamad Fuzi;* ***data collection:*** *Nur Naufal binti Aznan;* ***analysis and interpretation of results:*** *Nur Naufal binti Aznan, Siti Fatimah Zaharah binti Mohamad Fuzi;* ***draft manuscript preparation:*** *Nur Naufal binti Aznan, Siti Fatimah Zaharah binti Mohamad Fuzi. All authors reviewed the results and approved the final version of the manuscript.*

*The author confirms sole responsibility for the following: study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.*

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