Analysis of the ability of nano-mixture of *Coriandrum sativum* L. and *Mimosa pudica* L. leaves ethanol extract in lowering blood glucose and malondialdehyde (MDA) increased superoxide dismutase (SOD) in hyperglycaemic Wistar rats

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**ABSTRACT**

Introduction: Nano-mixture chitosan was used as a nano-extract framework, while tripolyphosphate was used as a stabilizer. *Coriandrum sativum* L. and *Mimosa pudica* L. nano extracts were created using the ionic gelatin technique. This study aimed to evaluate the effect of nano-mixture herbal extract of *Coriandrum sativum* L. and *Mimosa pudica* L. to lower free radicals and glucose levels in streptozotocin-induced hyperglycaemic rats.

Methods: Fourier transformation infrared (FTIR) characterized the resultant nano-mixture extract. The antihyperglycemic characteristics of a nano-mixture extract were investigated in streptozotocin-induced rats using a randomized post-test-only control group design. At the same time, blood glucose levels and oxidative stress markers MDA and SOD were monitored.

Results: *Coriandrum sativum* L. and *Mimosa pudica* L. extracts included polyphenols, flavonoids, alkaloids, and terpenoids, according to the results of the phytochemical test. Nano extract was well supported by PSA characterization as a delivery vehicle for bioactive chemicals, with a zeta potential of -23.98 mV and a particle size of 422.20 nm. The oral administration of the nano-mixture extract at a dose of 50 mg/Kg BW/day had the greatest results for lowering glucose blood MDA and raising SOD levels in hyperglycaemic rats, according to the antihyperglycemic test on streptozotocin-treated rats.

Conclusion: In hyperglycaemic rats, a nano-mixture of *Coriandrum sativum* L. and *Mimosa pudica* L. nano extract may lower MDA and blood glucose while raising SOD levels.

Keywords: *Coriandrum sativum* L., *Mimosa pudica* L., hyperglycaemic, nanoparticle.

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**INTRODUCTION**

Hyperglycemia, or persistently high blood sugar levels, is the hallmark of diabetes mellitus, a chronic illness brought on by problems with insulin action, production, or both. Oxidative stress is caused by an imbalance in the body’s synthesis of endogenous antioxidants and free radicals, which is brought on by high blood sugar levels. Although many distinct types of free radicals exist, reactive oxygen species (ROS) are the most common in the body’s biological systems. When a molecule’s covalent connection or an atom’s lone electron pair undergoes homolytic breakdown, these free radicals are created.

For decades, Indonesian has been consumed as fruits and vegetables containing numerous phenolic and flavonoid components with significant antioxidant activity. Indonesia is rich in biodiversity and contains antioxidant chemicals. Flavonoid chemicals can collect ROS, block the action of enzymes that create ROS and interact with healthy cells to prevent lipid peroxidation and deoxyribonucleic acid (DNA) damage.

The production of injured pancreatic cells, increased insulin secretion, and increased antioxidant enzyme activity are all attributed to flavonoids. By scavenging free radicals and decreasing oxidative stress and ROS, flavonoids assist antioxidant enzymes in controlling blood sugar levels and preventing hyperglycemia-related problems. *Coriandrum sativum* L. and *Mimosa pudica* L. are two of the 419 plant species from 133 plant groups listed by Marella, 2017 as having antidiabetic action. *Coriandrum sativum* L. and *Mimosa pudica* L. species were detected in a nano-mixture. Apigenin is a flavonoid derivative chemical extensively dispersed in nature and may be found in large quantities in various plants and fruits, in addition to having a hypoglycemic impact.

The ethanolic extract of coriander seeds and *Mimosa pudica* L. seeds were detected using liquid chromatography-mass spectrometry (LC-MS/MS).
utilizing LC-MS/MS for identification, numerous peaks of the chromatographic spectrum with various retention durations were obtained. A tiny syringe was used to inject up to 5 L of an ethanol extract sample of coriander and mimosa seeds made using the SPE technique and methanol eluent. The resulting chromatogram is then compared to the database using the MassLynx tool, which calculates the chemical’s mass, predicts the compounds in the spectra, and estimates the chemical’s mass. By contacting the website www.chemspider.com for the compound’s name and structure, the obtained molecular formula was then utilized to anticipate the substances in the ethanol extract of coriander seeds. Three active compounds were identified in the chromatogram of an ethanolic extract of coriander seeds: apigenin, 2-flouren-9-ylidenemethylpyridine, and anti-diabetic 5-Pentyl-1,3-benzenediol. 

Solid colloidal nano-mixture materials can be a medication delivery agent since their active ingredients have been dissolved, entangled, and encapsulated. Using a nano-mixture delivery method makes it easier for medications to move throughout the blood and take action swiftly. Chitosan polymer is a nanomaterial frequently employed as a safe medication delivery system for humans. Chitosan that had been triplyphosphate-ionic crosslinked just slightly swelled. Modifying the cross-linked chitosan to perform the desired function is also simple. Such as crystallinity, density, and hydrophilicity. The chlorofluro nano fraction of Kaempferia rotunda was also made effectively using the ionic gelation technique in combination with chitosan and sodium tripolyphosphate. Particle sizes that range from 172 to 877 nm and have zeta potential values between +28.06 mV and 38.03 mV are the findings of the investigation of the particle sizes. 

Based on the information provided above, the researcher examined and tested the effects of a nano-mixture of Coriandrum sativum L, Mimosa pudica L, chitosan, triplyphosphate, and chitosan on the levels of superoxide dismutase (SOD), blood sugar, and malondialdehyde (MDA). Because of their capacity as antioxidants to absorb ROS, they hinder the activity of ROS-producing enzymes that protect lipophilic antioxidants from ROS and promote a rise in enzymatic antioxidants. 

The restricted availability of flavonoids in the metabolic system is mostly due to poor digestive tract absorption and significant colon biotransformation. Flavonoids perform a variety of tasks in many biological processes. Furthermore, the bioavailability of flavonoids will be increased by creating a nano-mixture of chitosan, triplyphosphate, Coriandrum sativum L, and Mimosa pudica L extract ethanol, improving the transport system, metabolic stability, and shifting the absorption site from the large to the small intestine. The solubility and bioavailability of the bioactive compounds will be increased by the nano-mixture of chitosan, triplyphosphate, coriander (Coriandrum sativum L.), and mimosa (Mimosa pudica L. extract ethanol), allowing for a good and more stable effect to be produced at lower dosages. 

In hyperglycemic Wistar rats, this nano-mixture-chitosan-tripolyphosphate-Coriandrum sativum L. and Mimosa pudica L. extract ethanol was shown in vivo by observing an increase in superoxide dismutase (SOD) levels and a decrease in malondialdehyde (MDA) and blood glucose levels with nano-mixture chitosan triplyphosphate consumption. Chitosan is used as a scaffold for the nano-extracts of Coriandrum sativum L. and Mimosa pudica L, and triplyphosphate is added as a stabilizer using the ionic gelation technique. By detecting changes in the MDA and SOD biomarkers of streptozotocin-induced hyperglycemic Wistar rats, this study aimed to produce a nano-mixture of chitosan-tripolyphosphate Coriandrum sativum L. and Mimosa pudica L. as nano herbs to regulate the glucose level of these animals. Coriandrum sativum L. and Mimosa pudica L. extracts were used to characterize the physical-chemical characteristics of the nano-mixture using FTIR and zeta potential with PSA.

METHODS
Tools and Materials
Coriandrum sativum L. was purchased in the Kumbasari market in Denpasar, Bali, Indonesia. Mimosa pudica L. was collected from farms in Gianyar. They were discovered in Bali’s Eka Karya Botanical Gardens’ LIPI UPT Plant Conservation Center. Ingredients included 96% ethanol, distilled water, streptozotocin (Sigma Aldrich), chitosan, triplyphosphate, and filter paper. Male Wistar rats weighing 150-200 g and aged 2-3 months were utilized as experimental animals in this investigation.

Ethanol extract mixture of Coriandrum sativum L and Mimosa pudica L
Maceration of Coriandrum sativum L. and Mimosa pudica L. with 96% ethanol for 48 hours was performed, and the solvent was evaporated at 450°C as a result of the maceration. Following that, the moisture content (7.55%) was calculated. The water content of herbal medication should not exceed 10%, according to the criterion for simplicia. This extract was mixed with nano-chitosan-tripolyphosphate to explore the effects on blood glucose, MDA, and SOD levels.

Manufacture of nano-mixture
A one-gram thick extract made from ethanol of Coriandrum sativum L. and Mimosa pudica L. has been measured and diluted in 50 mL of 96% ethanol before being mixed with distilled water (100 mL) in 100 mL of 1% glacial acetate, 1 gram of chitosan was dissolved, and 1 gram of triplyphosphate was dissolved in 100 mL of distilled water. After that, the three solutions were mixed and stirred for two hours with a magnetic stirring apparatus. Centrifugation was used to separate nanoparticles of chitosan-tripolyphosphate-coriander seed extract. The recovered particle was separated and kept in a -4°C freezer for two days. Storage is moved to a refrigerator (300°C) until dry.

Size of Coriandrum sativum L and Mimosa pudica L as medicine
Extrasts of Coriandrum sativum L. and Mimosa pudica L. were used to determine the nanoparticle Zeta Potential Value. The substance was pumped into the cuvette until the bubbles were empty of bubbles. The intake is then covered to prevent vibration from interfering with the
findings. The cell penetration is in front of the cell support arrow. Furthermore, the electrode cell is examined to confirm that it is properly attached to the instrument electrode and that the tool cover is properly positioned. Then, from the drop-down option, select “Measurement start”. The cells were removed and cleaned when the measurements were finished.

**Blood glucose, malondialdehyde, and superoxide dismutase level measurement**

Blood glucose levels are reduced when assessed in mg/dL in rats' tail vein blood using the GLUCO method. Two treatments were carried out using a QuantiChrom TMT BARS test kit (DTBA-100) and the thiobarbituric acid reactive substance (TBARS) method according to the manufacturer’s instructions. The MDA levels were averaged. Activity test Kit (Hydroxylamine Method) biochemical test reagent was used in two treatments. The SOD test results are read at 450 nm using a microplate reader.

**Data Analysis**

ANOVA was used to examine the data. If the results were significant, a post hoc LSD test was used to compare the impact of Coriandrum sativum L. and Mimosa pudica L. extracts in each group. To identify which group had a significant outcome, post-hoc analysis was performed. SPSS version 24 was used for analysis.

**RESULTS**

**Coriandrum sativum L. and Mimosa sativum L. extract**

147.25 g of thick blackish-dark yellow ethanol extract with a yield of 7.55% was generated after 48 hours of maceration with ethanol solvent of 2000 grams of powdered Coriandrum sativum L. The solvent was ethanol because Coriandrum sativum L. and Mimosa pudica L. powder's water content surpassed the simplicia criteria. Excess water concentration in the simplicial may promote microbial development, cause hydrolysis of active chemicals, and make the extraction solvent less efficient. 

![Figure 1. Reduce blood glucose levels (K0: Streptozotocin induction, feed and drink). P1: 15 days later, streptozotocin induction, and diet Coriandrum sativum L. and Mimosa pudica L. extract ethanol. P2: 15 days later, streptozotocin induction, and diet nano chitosan-tripolyphosphate-Coriandrum sativum L. and Mimosa pudica L. extract ethanol.](image)

**Decrease in blood glucose level**

In particular, the blood glucose levels after day 3 of streptozotocin induction and after receiving one dosage of each ethanol extract every day for 15 days are presented in Figure 1, together with the blood glucose level profile of Wistar rats. The Wistar rats were given nano chitosan-tripolyphosphate-Coriandrum sativum L. and Mimosa pudica L. on the 15th day. The rats administered the Coriandrum sativum L. and Mimosa pudica L. ethanol extract at a dosage of 50 mg/kgBW had an average blood glucose level of 323.7 mg/dL in the control group K0 (only streptozotocin-induced). A group of rats was administered coriander seed and Mimosa pudica L. ethanol extract nano-mixture particles at a dosage of 50 mg/kgBW, and their average blood glucose
level was 136.33 mg/dL. The intermediate blood glucose level in Group P2 was 99.4 mg/dL.

Decrease in malondialdehyde level

Figure 2 depicts the groups of rats that received a 50 mg/kg BW dosage of nano chitosan-tripolyphosphate-Coriandrum sativum L. and Mimosa pudica L. This study found a significant difference (p<0.05). Further testing was performed to determine which groups differed from the control group, and the results revealed that MDA and Wistar rats given the Ch-Tpp-Mp-Cs nano-mixture had lower MDA levels than Wistar rats given either Ch-Tpp or Mp-Cs nano. This demonstrates that Ch-Tpp-Mp-Cs outperforms Ch-Tpp and Mp-Cs nano as an antihyperglycemic drug. Ch-Tpp and Mp-Cs nano synergize as antihyperglycemic substances since they include flavonoids. Free radicals and oxidative stress influence the development of hyperglycemia.

Increase in superoxide dismutase (SOD)

SOD levels were evaluated during streptozotocin induction (K0), streptozotocin induction + ethanol extracts of Coriandrum sativum L. and Mimosa pudica L. (P1), and streptozotocin induction + Ch-Tpp-Mp-Cs (Chitosan-Tripolyphosphate-Mimosa pudica L.-Coriandrum sativum L.) (P3). As shown in Figure 3, this study found a significant difference (p<0.05). Further tests were done to establish which groups varied from the control group, and the findings show that the SOD levels of the Wistar rats administered Ch-Tpp + nano Coriandrum sativum L. and Mimosa pudica L. extract ethanol (P2) were greater than the SOD levels of the control group. This suggests that Ch-Tpp + nano Coriandrum sativum L. and Mimosa pudica L. extract ethanol is more effective as an antihyperglycemic drug. Ch-Tpp and Mp-Cs, which include flavonoids, work synergistically as antihyperglycemic agents.

The chromatogram in the figure reveals 11 peaks with varying retention times, showing that the coriander seed ethanol extract may include 11 different types of compounds. Following the examination, only seven mountains were discovered. The LC-MS/MS analysis of Coriandrum sativum L. extract ethanol produced a chromatogram with seven retention time peaks (3,991; 3.991; 7,703; 8,603; 8,664; 9,883; 10,815 minutes).

Characterization with particle size analyzer (PSA)

A particle size analyzer (PSA) is used to evaluate a basic material’s zeta potential value and particle size. The zeta potential of nano chitosan-tripolyphosphate-Coriandrum sativum L. extract ethanol is 25.80 mV, indicating that it might be used to introduce bioactive chemicals. The nano chitosan-tripolyphosphate particle size is 119.3nm, suggesting it has the most surface area of the three samples.

Table 1. Zeta potential and particle size

<table>
<thead>
<tr>
<th>Sample</th>
<th>Zeta Potential (mV)</th>
<th>Particle Size (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coriandrum sativum L. and Mimosa pudica L. extract ethanol</td>
<td>-2.40</td>
<td>624.8</td>
</tr>
<tr>
<td>Nano chitosan-tripolyphosphate</td>
<td>-8.40</td>
<td>119.3</td>
</tr>
<tr>
<td>Nano-mixture chitosan-tripolyphosphate-Coriandrum sativum L. and Mimosa pudica L. ethanol extract</td>
<td>-23.98</td>
<td>442.2</td>
</tr>
</tbody>
</table>
DISCUSSION

Coriandrum sativum L. and Mimosa pudica L. samples were macerated in 96% ethanol. The ethanol extract of Coriandrum sativum L. with Mimosa pudica L. yielded 14.74% (w/w). The phytochemical analysis of Coriandrum sativum L. and Mimosa pudica L. extracts revealed that they included polyphenol chemicals, flavonoids, and alkaloids. Because the OH-group on the polyphenol molecule combines with Fe³⁺ ions in the FeCl₃ reagent to generate the complex product Fe(Phenol)Cl₂ [16], the color changes from brownish red to black. Mg and HCl function in the flavonoid test with Wistletar reagent to reduce the benzopyran core of the flavonoid structure, producing air bubbles and the emission of H₂ gas. The presence of antihyperglycemic secondary metabolites and antioxidants is suggested to have reduced blood glucose levels in Wistar rats. Hyperglycemia elevates oxidative stress while lowering endogenous antioxidants (antioxidants generated by the body). Consuming natural antioxidants helps to prevent diabetes by preventing peroxide reactions that injure pancreatic beta cells. According to Yulianty, 2015, Coriander seeds include many helpful chemicals that help decrease blood glucose levels. Polyphenolic chemicals, alkaloids, and flavonoids were discovered using phytochemical screening.

Many ROS generated by human metabolism interact with double bonds and fatty acids to form MDA, which promotes lipid peroxidation on cell membranes. Creating free radicals such as H₂O₂ and hydroxyl radicals in cell membranes contributes to developing lipid peroxides (MDA). According to the average drop in blood MDA levels in hyperglycemic rats, phenolic substances such as flavonoids, saponins, alkaloids, and terpenoids can lower blood MDA levels in Wistar rats by oxidizing unsaturated fatty acids in long-chain lipids. Consequently, as an antihyperglycemic drug, the Ch-Tpp-Mp-Cs nano-mixture beats Ch-Tpp and Mp-Cs nano. Cs and Mp, including flavonoids, function synergistically as antihyperglycemic drugs. SOD activity may be utilized to calculate oxidative stress in the body.

The substance is thought to be apigenin, according to the database. Figure 4 depicts the compound’s structure. Apigenin, a chemical, is believed to exist. Apigenin is a flavonoid derivative compound found in abundance in nature, including celery, onions, chamomile flowers, oranges, and tea leaves, and it has the potential to be an anti-cancer, anti-inflammatory, and antioxidant compound with intrinsic toxicity. The lowest. Flavonoids are antioxidant chemicals that help in diabetes control. The flavonoid-derived apigenin molecule was suspected of having antihyperglycemic potential in this investigation.

For several hours, the viscous gel sheath that surrounds the nano-chitosan-tripolyphosphate-Coriandrum sativum L. extract ethanol acts as a natural barrier for flavonoids to be released, aiding in preserving the flavonoids in dosage form until all of the flavonoids are removed. The gel form will be stored for several hours, delaying the release of flavonoids for an extended period. Fluid movement disrupts intermolecular interactions and opens the long structure of chitosan polymer chains. This slows the loading of the hydrogel layer on the surface of the nano chitosan-tripolyphosphate-Coriandrum sativum L. extract, allowing the flavonoids to be released within the gel layer. This study has several limitations, such as not including any confounding variables that might affect the results.

CONCLUSION

A nano-mixture of Coriandrum sativum L. and Mimosa pudica L. nano extract may reduce MDA and blood glucose levels while increasing SOD levels in hyperglycemic rats. Nano extracts are made by encapsulating bioactive substances from Coriandrum sativum L. extract ethanol with chitosan and tripolyphosphate polymer as material for encapsulation framework for extensively developing delivery systems for bioactive substances in the medical field. Further studies are needed to validate these findings so that many of these findings can be applied to clinical settings. Further research on the release rate of bioactive substances encapsulated in nano chitosan-tripolyphosphate-Coriandrum sativum L. and Mimosa pudica L. extract ethanol and clinical trials regarding the activation of antihyperglycemic nano chitosan-tripolyphosphate-Coriandrum sativum L. and Mimosa pudica L. extract in humans is needed.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTION

The authors participate in the contemplation equally, comparing with the examination notions, content acquisitions, content investigation, factual investigations, modifying the paper, and lastly, describing the consideration through publication.

ETHICAL CONSIDERATION

This study was approved by the Research Ethics Committee, Faculty of Medicine, Udayana University, Denpasar, Bali, Indonesia, with the number of approval: 3892/UN14.5.2.VII.14/LT/2022.

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