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Anti-Inflammatory Activity of Dried Ginger Mediated Iron Nanoparticles

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Authors' contributions

This work was carried out in collaboration among all authors. Author SSLG designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author MJ managed the analyses of the study. Authors SP and SR managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Nanotechnology is a branch of science and technology relating to the matter on the atomic and molecular scale in the size range between 1-100 nm. Iron nanoparticles have diverse diagnostic and potential therapeutic applications with unique magnetic and catalytic properties and potent biological activities. The present study aimed to analyse the anti-inflammatory activity of iron nanoparticles synthesized from dried ginger. The synthesized iron nanoparticles were characterized using UV-vis spectroscopy and evaluated for anti-inflammatory activity by inhibition of albumin denaturation assay. The nanoparticles showed maximum absorbance at 360 nm and revealed potent anti-inflammatory effect with maximum of 83.5% inhibition at lowest concentration of 50 µl and thus can be used as an anti-inflammatory agent in various inflammatory diseases.

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1. INTRODUCTION

Nanotechnology is characterized by the examination and utilization of structures between 1 and 100 nm in size. Products based on nanotechnology in medicine has an enormous positive impact on human health by enhancing the efficacy and safety of nanosystems and nanodevices. (Paul and Robeson, 2008). Inflammation is the host response to any stimuli to the body such as physical, chemical or biological and is characterized by redness, swelling, pain and increased heat. Sometimes the persistence of inflammatory action itself may lead to more tissue destruction in the host. Macrophages and neutrophils play a crucial role in regulating inflammation in the pathogenesis of various diseases [1]. Mechanisms that are involved mainly in inflammatory process are prostaglandins released by cyclooxygenase (COX) and nitric oxide production (NO) by nitric oxide synthase [2]. Inhibition of cyclooxygenase pathway is the mechanism by which non-steroidal anti-inflammatory drugs work which are used in the treatment of several inflammatory diseases. The two isoforms of COX namely COX-1 contribute to physiological functions and COX- 2 responsible for inflammation. Among the various plant based materials that show anti-inflammatory effect, gingerol related compounds in *Zingiber officinale* (ginger) were found to inhibit cyclooxygenase-2 (COX-2) three-fold more than cyclooxygenase-1 (COX-1) [3]. The first revelation of ginger's inhibitory consequences for prostaglandin biosynthesis in the mid-1970s has been affirmed. This disclosure distinguished ginger as a home grown medicine that imparts pharmacological properties similar to non-steroidal anti-inflammatory drugs [4].

A significant expansion of this early work has revealed that the gingerols and diarylhepatanoid as active compounds that inhibited leukotriene synthesis by hindering 5-lipoxygenase [5-6]. This disclosure of ginger acting as inhibitors of COX-2 and 5-lipoxygenase may have a superior anti-inflammatory with less toxic effects [7]. There are numerous studies available on green synthesis of nanoparticles and evaluated its biological properties [8-14]. Nonsteroidal anti-inflammatory drugs (NSAIDs) are currently the most widely used drugs in the treatment of inflammatory diseases. These drugs may result in adverse side effects and damage the human biological system such as liver and gastrointestinal tract and may also affect the cardiovascular system. The anti-inflammatory activity has been reported to be exhibited by various metal and metal oxide nanoparticles as these are shown to have better penetrating action into cells and good ligand-binding properties (Agarwal H 2019). Iron nanoparticles empowered with superior magnetic and electric properties can be synthesized by green approach which is more convenient, compatible and non –toxic. Iron oxide nanoparticles has been shown to suppress the synthesis of pro-inflammatory cytokines namely, IL-1β and TNF-α by murine microglia when stimulated with lipopolysaccharides [15]. Iron nanoparticles biosynthesized from *Juglans regia* water extract showed highest albumin denaturation assay at 400 µg/ml [16]. The present study focused on synthesizing iron nanoparticles mediated by dried ginger and analysing its anti-inflammatory activity.

2. MATERIALS AND METHODS

2.1 Preparation of Dried Ginger Extract

Zingiber officinale (ginger) was procured from the local market and shade dried. The dried ginger is crushed and powdered. To prepare the dried ginger extract, 50 mL of distilled water was taken in a conical flask and 0.5 g dried ginger powder was mixed to the distilled water. The solution was labeled and heated in the mantle at a temperature of 50-60°C for 5 minutes. After the heating process the solution was filtered using whatman grade 1 filter paper to obtain the final extract.

2.2 Synthesis of Nanoparticles

To synthesize iron nanoparticles, 0.324 g of iron chloride anhydrase was taken and added to 60 mL of distilled water. The solution was then added to 40 mL of dried ginger extract that has been prepared before. The solution was observed to be brown in colour. Further the extract solution was clogged with a foil paper and placed in an orbital shaker. The colour changes of the solution were observed at various periods of time for 36 h in an interval of 2 h. After complete synthesis the solution was made to dry by gently heating in the furnace. The annealed powder was considered as the samples of the study.

Fig. 1. Synthesis process of iron nanoparticles from the extract of dried ginger

2.3 Characterization of Iron Nanoparticles

The synthesized iron nanoparticles were characterized by UV-vis spectroscopy. This absorption spectroscopy method is used for determination of wavelength at visible ranges affecting the color of the bioactive compounds. The synthesized iron nanoparticles from dried ginger were optically measured at different wavelength ranging from 250 nm to 650 nm.

2.4 Inhibition of Albumin Denaturation Assay

Bovine serum albumin (BSA) was used as a reagent for the assay. BSA comprises roughly 60% of all proteins in animal serum. To 2 mL of 1% bovine albumin fraction, dried ginger mediated iron nanoparticles in different concentrations (10-50 µl) was added and the pH of reaction mixture was adjusted to 6.8 using 1 N HCl. The reaction mixture was incubated at room temperature for 20 minutes and then heated at 55°C for 20 minutes in a water bath. The mixture was cooled to room temperature and the absorbance value was recorded at 660 nm (Fig. 2). An equal amount of dried ginger powder was replaced with DMSO (Dimethyl sulfoxide) as standard. Assays were done in triplicate; thus, inhibition percentages were the mean of three observations. The % Inhibition was calculated for each concentration by the given formula:

$$\% \text{ Inhibition} = \frac{\text{Control O.D} - \text{sample O.D}}{\text{Control O.D}} \times 100$$

Fig. 2. Anti- inflammatory activity of dried ginger mediated iron nanoparticles carried out by inhibition of albumin denaturation assay

3. RESULTS AND DISCUSSION

3.1 Visual Identification

From the iron nanoparticles synthesized using *Zingiber officinale*, the change in the colour was recorded at various time periods. Iron nanoparticles exhibited yellowish-brown color in aqueous solution. Fe^{2+} ion reduction process was observed by direct visual observation of the solution. After 36 h, conversion of yellow to dark brown occurred.

3.2 UV Visible Spectroscopy

The UV-vis spectroscopy analysis of the iron nanoparticles was made in the range of 250 to 650 nm. The absorption peak was found to be at 360 nm within 48 h. The surface plasmon resonance is characteristic of the reduction of Fe^{2+}ions mediated by dried ginger during the synthesis process. After 48 h no further reduction of metal ions occurred indicating the complete synthesis of iron nanoparticles. The phytocompounds present in the dried ginger may be the reason for the stability of the iron nanoparticles and facilitation of reduction of Fe^{2+} ions [17]. The characteristic absorption peak obtained in our study was in accordance with previous studies of biogenic synthesis of iron nanoparticles with reference to maximum absorption range of 300 – 500 nm [18], 256 nm – 277 nm [19]. The UV- vis spectroscopic analysis of iron nanoparticles from garlic and ginger revealed maximum absorption peak at 280 nm [17].

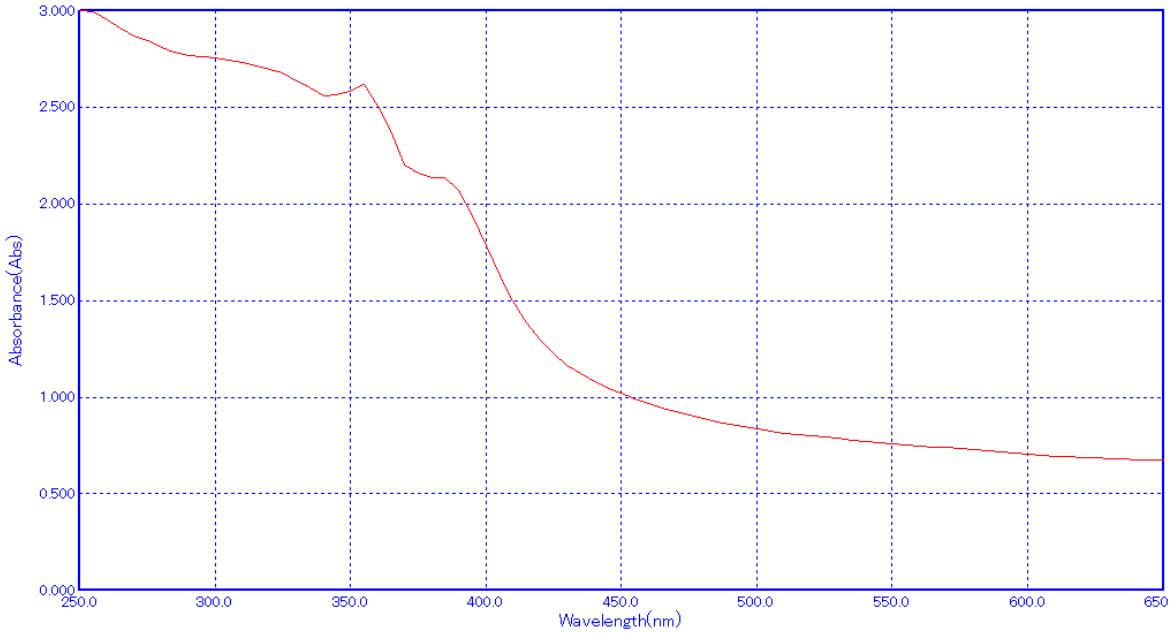

Fig. 3. UV-vis spectroscopy of iron nanoparticles synthesized from extract of *dried ginger* recorded as function of time

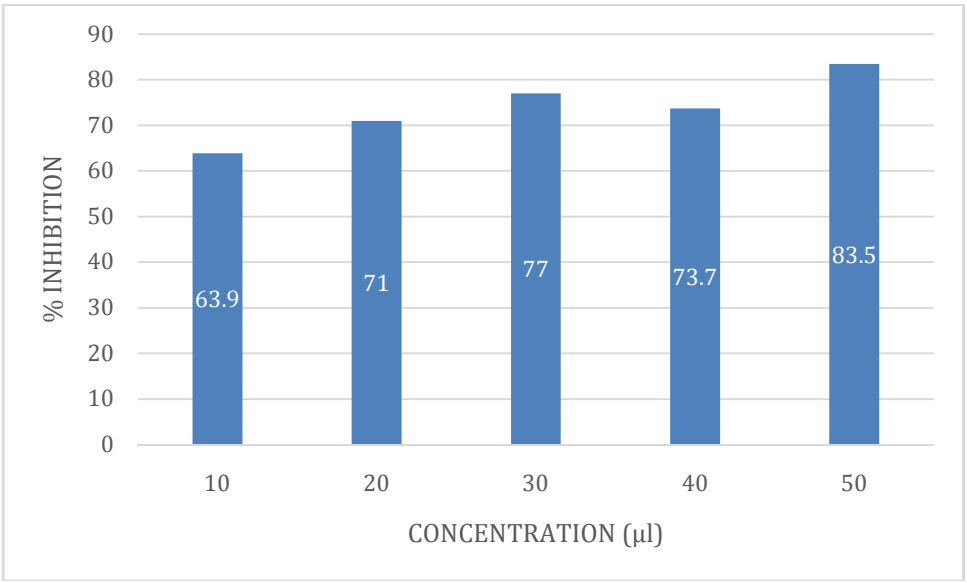

Fig. 4. The quality of anti-inflammatory activity of dried ginger mediated iron nanoparticles

3.3 Anti- Inflammatory Action

The anti-inflammatory action of the dried ginger concentrate was estimated by the inhibition of albumin denaturation assay. The present study showed that the % inhibition was maximum at 50 µl concentration showing 83.5% inhibition of albumin denaturation and lowest % inhibition at 10 µl concentration when comparing to the standard. The synthesized dried ginger mediated iron nanoparticles revealed maximum quality of anti-inflammatory activity at 50 µl concentration with % inhibition of 83.5%.

The nanoparticles being smaller in size can penetrate through intact mucosal barriers and can interact with the plasma proteins forming protein corona around the nanoparticles based on its physical properties. The protein corona has serum proteins acting as a ligand for the M2

macrophage receptors. It is reported that nanoparticles rapidly uptake M2 macrophages which show anti-inflammatory effect than M1 macrophages [1].

The previous literatures have showed potent anti-inflammatory activity of iron nanoparticles from plant based materials. The anti-inflammatory effect of iron nanoparticles synthesized from the aqueous leaf extract of *Ocimum tenuiflorum Linn.* showed maximum anti-inflammatory activity at 100 mg/mL [20]. In the present study, the anti-inflammatory activity was more effective in in vitro by incorporating nanoparticles mediated by dried ginger which cause inhibition of COX-2 pathway by the gingerol related compounds and the anti-inflammatory effect of M2 macrophages brought down by protein corona formed by the nanoparticles.

4. CONCLUSION

The present study has demonstrated an eco-friendly and cost-effective synthesis of nanoparticles synthesized from dried ginger. This was initially identified by stable dark brown colour and the surface plasmon resonance positioned peak at 360 nm. The synthesized dried ginger mediated iron nanoparticles showed potent anti-inflammatory effect with maximum inhibition of 83.5% at 50 µl concentration and hence can be used as an anti-inflammatory agent in various pathological diseases at this optimal concentration.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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