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Original article

Green synthesis of silver nanoparticles using aqueous rhizome extract of *Zingiber officinale* and *Curcuma longa*: In-vitro anti-cancer potential on human colon carcinoma HT-29 cells

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ABSTRACT

This study was aimed to analyze the anti-cancer activity of silver nanoparticles (AgNPs) synthesized using aqueous plant extracts from the rhizome of *Curcuma longa* and *Zingiber officinale*. Synergistic aqueous extract of rhizome of *C. longa* and *Z. officinale* was used to green synthesis of AgNPs. Characterization of AgNPs was performed using UV–visible spectroscopy, FTIR, X-ray diffraction, TEM, and SEM analyses. Anti-cancer activity of AgNPs against human colon carcinoma (HT-29) cells was tested using MTT assay. UV–Visible spectroscopy analysis indicated the surface plasmon resonance (SPR) sharp peak at 350–430 nm wavelength that corresponds to the production of AgNPs. FTIR analysis reveals that existence of carboxyl (—C═O) and amine (N—H) functional groups in the AgNPs. The X-ray diffraction analysis confirms four spectral peaks at 111, 200, 220, and 311. SEM analysis showed that AgNPs are in a spherical shape with a size of 42–61 nm and TEM analysis showed particle size are ranged between 20–51 nm. Anti-cancer study reveals that AgNPs had shown cytotoxicity against HT-29 cells at the concentrations ranged from 25 to 500 μg/mL and IC_{50} at 150.8 μg/mL. This study concludes that AgNPs synthesized using rhizome of *Z. officinale and C. longa* possesses potential anti-cancer activity.

1. Introduction

Medicinal plants are being used for human health care management in traditional medicine for centuries. High demand in the products from medicinal plants increased the commercial production and formulation of various herbal-based cosmetics and nutritional supplements (Ekor. 2014). Zingiberaceae family has around 52 plant genera and more than 1300 plant species, and also, many of these plant products were in use for various human health benefits (Kress et al., 2002). Some of the Zingiberaceae plants were reported for their therapeutic usage (Basak et al., 2010). Among those, *Curcuma longa* and *Zingiber officinale* are the most important medicinal plants, and they have possessed a variety of medicinal values. *C. longa* is an aromatic plant, commonly known as turmeric. In Ayurveda and Siddha, the vegetal root of *C. longa* has been used for the production of various pharmaceutical formulations for the different ailments, including wounds, acne, common cold, parasitic infections, urinary tract infection, and liver diseases (Chainani-Wu, 2003). This plant also possesses various important medicinal properties like antioxidant, anti-inflammatory, antibacterial, anti-human immunodeficiency virus properties (Araújo & Leon, 2011; Boaz et al., 2011). Polyphenol curcumin is a vital phytocompound responsible for the pharmacodynamics action of *C. longa* (Zhang

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et al., 2012; Sharma et al., 2005). Mainly, it has potential anti-cancer property against liver, pancreatic, colon, cervical, lung, brain, breast, and bone cancers (Maheshwari et al., 2006; Bar-Sela et al., 2010).

Another most important medicinal plant is *Z. officinale*, generally called as Ginger. The rhizome of this plant is widely used as a nutraceutical and in the formulation of folk medicine. In Ayurvedic and Chinese traditional systems of medicines, *Z. officinale* has being used for treating indigestion, arthritis, rheumatism, fever, and microbial infections (Darvesh et al., 2012). Asgingerols, zingerone, shogaols, paradols, and gingerdiols are the major phytochemical constituents that have been reported for its antioxidant, anti-inflammatory, anti-hyperglycemic, immunomodulatory, anti-cancer, and cardioprotective properties (Shehzad et al., 2013; Scalbert et al., 2005).

Medicinal plants based synthesis of nanoparticles has various biological benefits since they have no toxic chemicals and biological compounds as capping agents (Garima et al., 2011). Plant-based synthesized AgNPs are having strong antimicrobial activity and they are widely used as an ingredient in the pharmaceutical industry for preparation of human health care medicines (Manach et al., 2004; Ali et al., 2008). Biological synthesis of NPs is an environmental friendly method than chemical, electrochemical (Nicoll and Henein, 2009), radiation (Li et al., 2012), photochemical methods (Rhode et al., 2007). The biological and medicinal properties of NPs are mostly determined by various physical properties like particle size, structure, and crystallinity composition. AgNPs are interacting with cells and regulate active and passive cellular responses. AgNPs also cause DNA damage and chromosomal aberrations at a low concentration without toxicity, especially no genotoxicity effects on human cells (Zhang et al., 2016a,b; Gurunathan et al., 2018). Since the usage of AgNPs as a drug carrier in cancer treatment has recently gained considerable attention (Brahmbhatt et al., 2013). In this study, AgNPs synthesized using synergistic aqueous extracts of the rhizome of *Z. officinale* and *C. longa* were used for analyzing *in vitro* anti-cancer activity against human colon carcinoma (HT-29) cells.

2. Materials and methods

2.1. Collection of plant and preparation of extracts

The rhizome of *Z. officinale and C. longa* was collected from the region of Tiruvallore District, Tamil Nadu, and India. Soil and other surface contaminants present on fresh rhizome were removed using tap water followed by distilled water. Further, the rhizome was air-dried and macerated to make a fine powder. Followed by 5 g of mixed rhizome powder of both the *Z. officinale* and *C. longa* was added into 250 mL of distilled water and boiled for 30 min. After cooling to room temperature, the extract was centrifuged at 5000 rpm, and filtered using Whatman number-1 filter paper (20–24 µm). Filtered extract was further used for green synthesis of AgNPs.

2.2. Green synthesis of AgNPs using rhizome extracts

The prepared extract was utilized for the synthesis of AgNPs. 20 mL of 1 M $AgNO_3$ solution was added into 80 mL of rhizome extract. Then extract along with optimized AgNPs was incubated until the colorless solution turns into brownish color, which reveals the reduction of Ag^+ into Ag^0 nanoparticle. The visible color change was observed at a 1:9 ratio.

2.3. Characterization of AgNPs

UV spectrum analysis was estimated using UV-1800 spectrophotometer (Shimadzu, Japan) with the wavelength range from 200 to 800 nm. AgNPs were further characterized using FTIR to identify the functional groups, dynamic light scattering (DLS) particle size analyzer, XRD for elemental composition, TEM, and SEM for identification of morphology and size of biosynthesized AgNPs (Karuppiah et al., 2014).

2.4. In-vitro cytotoxic activity of AgNPs by MTT assay

The cytotoxicity activity of AgNPs was performed using MTT assay (Kleemann, 1993) against HT29 cells. In this method, 200 µL HT29 cells, roughly 1×10^4 cells/well, were seeded into 96 well plates and permitted to achieve confluence cell growth. After cells were completely attached to the well, culture media was discarded. Further, 100 µL of various concentrations such as 25, 50, 100, 250, and 500 µg/mL of AgNPs were added and incubated for 24 h and followed for 48 and 72 h. After that, freshly prepared MTT [5 mg/mL of phosphate buffer solution] was added and incubated at 37 °C for 4–6 h.

3. Results and discussion

3.1. Visual analysis of AgNPs

Several studies evaluated the green synthesis of AgNPs by different medicinal plant aqueous extracts for increasing various biological applications (Li et al., 2007). It was observed that NPs synthesis was initiated once the synergistic aqueous extracts of *Z. officinale and C. longa* added in the 1 mM $AgNO_3$ solution. The color of AgNPs and *Z. officinale* and *C. longa* aqueous solutions was progressively modified from yellow to brownish color which reveals the AgNPs formation. The color transformation during the synthesis of AgNPs is related to the excitation effect of surface plasmon resonance (Mittal et al., 2014; Balaraman et al., 2020). The current study investigation reveals that AgNPs were synthesized using rhizome extracts and the phytocompounds in the extracts of *Z. officinale and C. longa* have potential for acting as a reducing agent.

3.2. UV–visible spectroscopy analysis

UV–visible spectroscopy was used to observe the AgNPs formation by the reduction of Ag ions through the exposure of plant extracts (Cittrarasu et al., 2019). UV–Visible spectroscopy indicated the surface plasmon resonance (SPR) sharp peak at 350–430 nm wavelength, which corresponds to the AgNPs production. AgNPs were absorbed radiation at 400 nm wavelength due to the transition of electrons. Colloidal AgNPs exhibit absorption wavelength at 390–420 nm (Naik et al., 2002). The SPR peak explained that NPS synthesized were poly-dispersed environmental particles (Firdhouse & Lalitha, 2015). AgNPs synthesis from various medicinal plants such as *Ocimum tenuiflorum*, *Centella asiatica,* and *Clonorchis sinensis* extracts and observed the absorbance at 420 nm using UV-spectrophotometer (Chung et al., 2016). In a study, maximum absorbance was reported at 440 nm in the NPs synthesis using *Plumbago zeylanica* and 400 nm in the *Catharanthus roseus* (Nayak et al., 2016). In our study, the spectrum analysis peak data [Figs. 1, 2] showing that the silver synthesized product is only AgNPs. In a study, AgNPs were effectively synthesized using *C. longa* extract, then *Z. officinale* even at higher concentrations, and NPs are stable (Majeed et al., 2016).

3.3. FTIR analysis

FTIR analyzed data of AgNPs and *Z. officinale,* and *C. longa* rhizome extracts are shown in [Figs. 1, 3]. FTIR characterization was

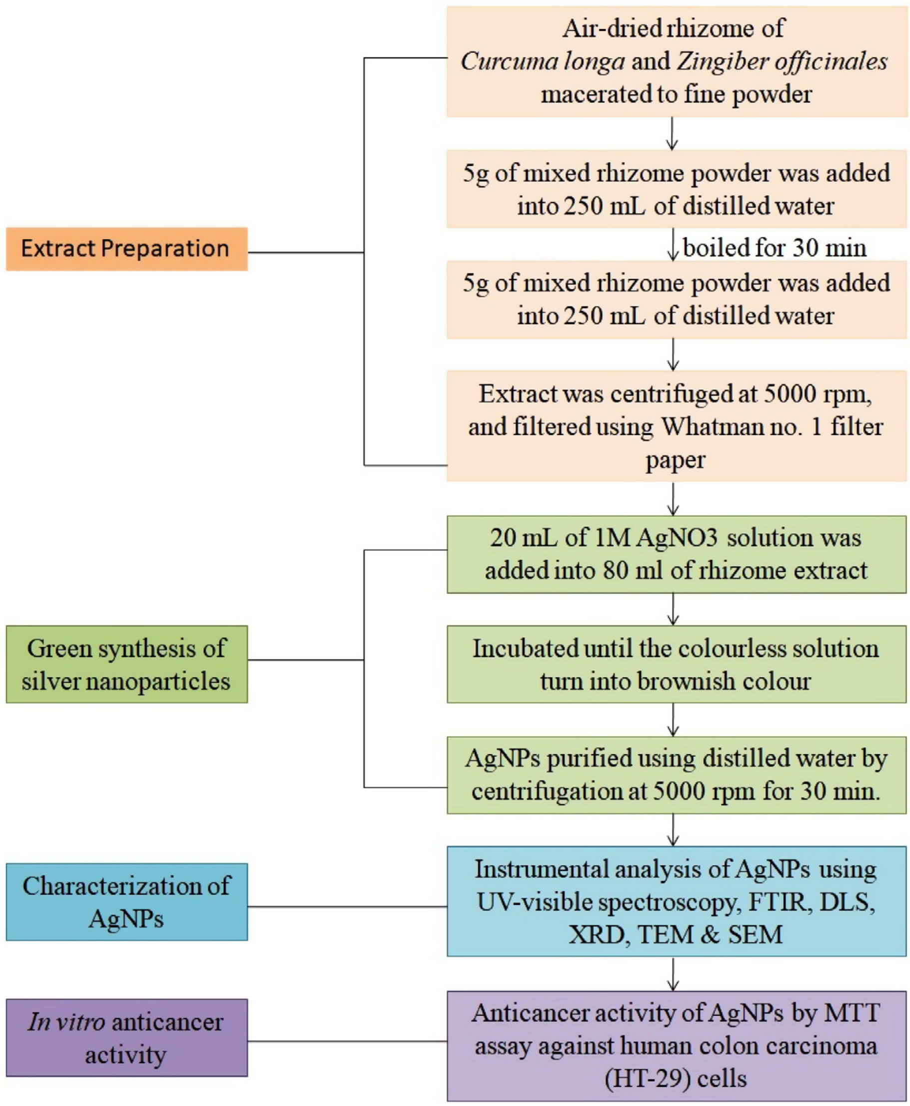

Fig 1. Flow chart of green synthesis of silver nanoparticles and anti-cancer study.

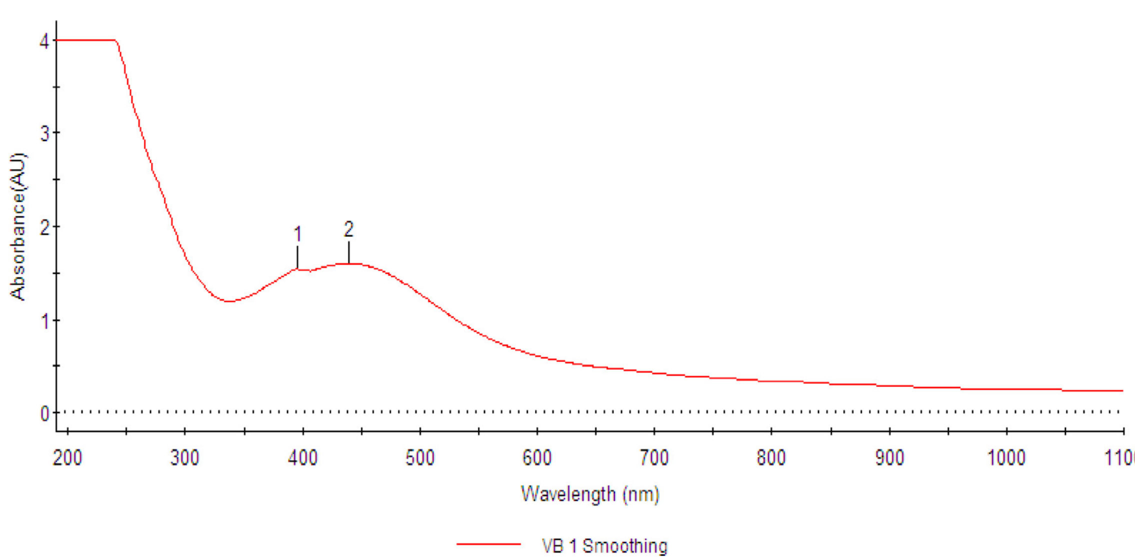

Fig 2. UV–Vis absorption spectra of green synthesized AgNPs.

used to examine the possible functional molecules, FTIR spectrum of the *Z. officinale* and *C. longa* rhizome extracts showed a major absorption peak at 1387 cm^{-1} in the synthesis of AgNPs (Logeswari et al., 2015). A report revealed that the presence of absorption peak at 1055 $cm^{-1,}$ which may have been attributed to vibration of (—C=O) and amine (N—H) groups (Jyoti et al., 2020; Kalaimurugan et al., 2019). The absorption peak appeared at 1459 cm^{-1} was specific for the vibration of proteins being a stabilizing agent through free amine groups or cysteine groups (Pirtarighat et al., 2019). In another study, FTIR spectra results identified the presence of amide groups in the fruit shell extract, and they were found to be involved in the reduction of silver ions to AgNPs. Additionally, plant phytocompounds perform double role functions (Gomathi et al., 2020).

3.4. Dynamic light scattering (DLS) studies

DLS technique makes use of particle size analysis of colloidal solution upon irradiating with the light source. The measurement condition was maintained at temperature 25 °C. From the DLS histogram [Figs. 1, 4], the average particle size is estimated to be 76.4 nm with a polydispersity index 0.325 and diffusion coefficient 6.438 x108 cm2/s, respectively.

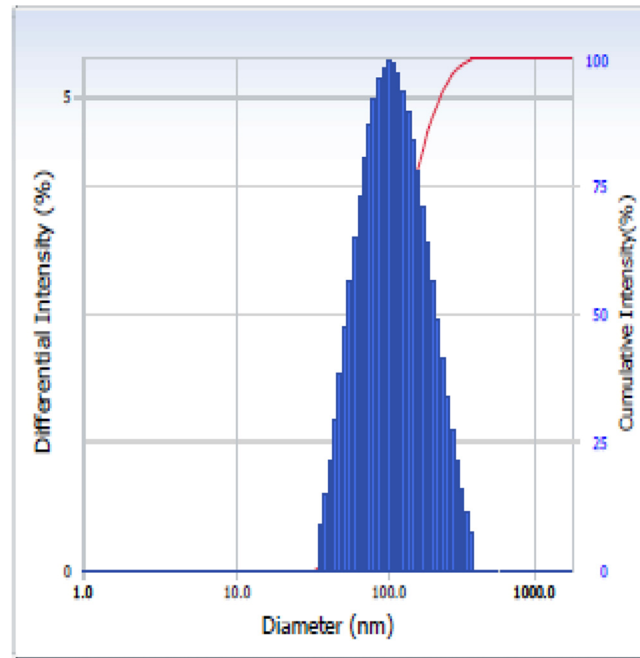

Fig 4. Dynamic Light Scattering (DLS) plot for green synthesized AgNPs.

3.5. XRD analysis

Vetrivel et al. (2019) synthesized crystalline AgNPs through green synthesis using *Ceropegia bulbosa* Roxb root tuber extract and observed XRD diffraction peaks at the 111, 200, 220, and 311 planes, which correspond to the AgNPs. Synthesized AgNPs were also confirmed for their antibacterial and larvicidal activity. In this study, the X-ray diffraction (XRD) patterns of the dried synergistic powder sample of green synthesized AgNPs had shown distinct four diffraction peaks at 2θ angles of 38°, 44°, 64°, and 77°, which can be endorsed to the reflections from lattice planes indexed to the (111), (200), (220), and (311) planes, reflected the crystal structures [Figs. 1, 5] (Ali et al., 2016; Paulkumar et al., 2014; Shankar et al., 2004) of AgNPs.

3.6. SEM analysis

SEM image provides morphological characteristics and size measurement of synthesized AgNPs [Figs. 1, 6] as reported by Rautela et al., (2019). The SEM size was examined the range of 41.91to 60.91 nm. A study reported that AgNPs synthesized using *Z. officinale* extracts were in spherical shape and size of 30–50 nm (Zhang et al., 2016a,b). These size variations might be the presence of biomolecules from the rhizome extracts, which were the caping surface of AgNPs. It was observed that AgNPs have a uniform crystalline structure and relatively spherical. Accumulation of NPs was induced by solvent evaporation during the sample production. In a study, SEM analysis of NPs synthesized using *C. longa* possess that the synthesized nanoparticle metals are spheri-

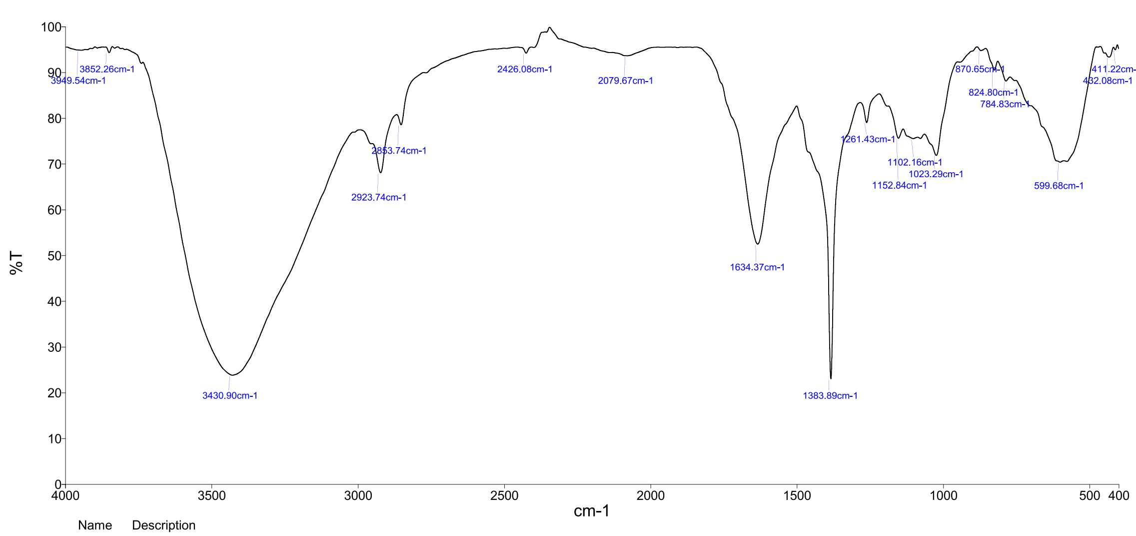

Fig 3. FTIR spectra of green synthesized AgNPs.

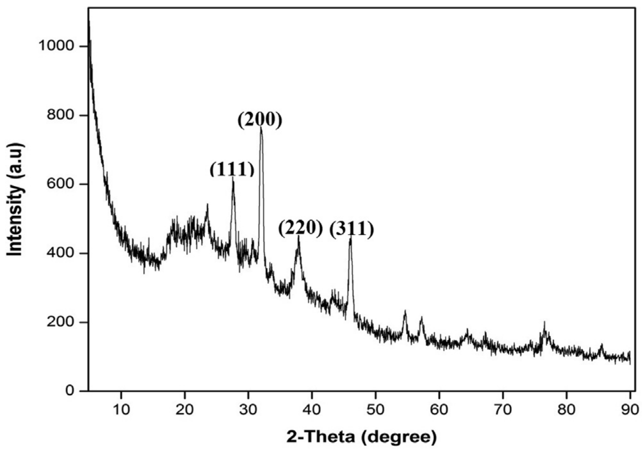

Fig 5. XRD spectrum of green synthesized silver nanoparticles.

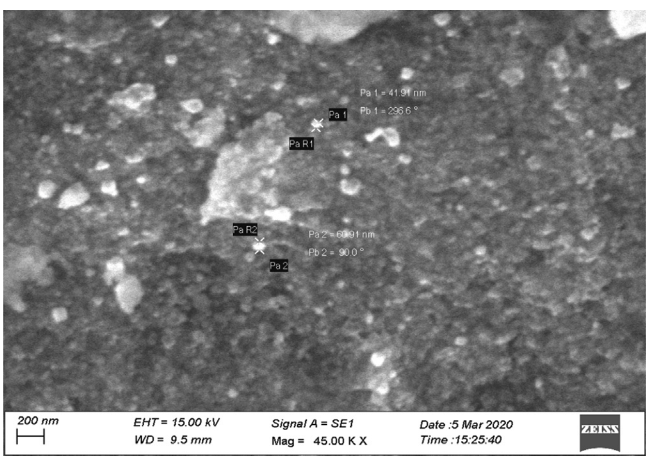

Fig 6. SEM images of green synthesized AgNPs.

cal in shape throughout in the colloidal solution (Aswathy and Philip, 2012).

3.7. TEM study

TEM microscopic analysis was used to determine the morphology and size distribution of biosynthesized AgNPs. The particle shape of the AgNPs is spherical, with ranged from 20 to 51 nm [Figs. 1-7]. Consuming the *Z. officinale* and *C. longa* extracts during the time lack the decrease of reducing agents, which lead to different size of AgNPs (Chandran et al., 2006; Dubey et al., 2010). In a study, microbial synthesis of AgNPs was carried out using *Pseudomonas fluorescens* YPS3 and observed the size of NPs as 26 nm. In our study, TEM analysis showed the smallest size of AgNPs synthesized was 20 nm (Kalaimurugan et al., 2019).

3.8. In-vitro anticancer activity of AgNPs using MTT assay

Colorectal cancer is the main primary colon cancer and it is the third most common cancer worldwide (Yin et al., 2003). In this present study, the cytotoxicity of green synthesized AgNPs was analyzed using MTT assay and found that AgNPs showed anti-cancer activity against colon cancer (HT29) cells at the concentration of 25–500 μg/mL. It was noted that cell viability was deceased on the increased concentration of AgNPs [Figs. 1, 8]. AgNPs required concentration to reduce the cell viability of HT29 cells to 50% (IC50) of the preliminary population was 150.8 μg/mL. The results showed dose-dependent cytotoxicity of human colon carcinoma cells after 24 h of AgNPs treatment since it was tested at various concentrations such as 25, 50, 100, 250, and 500 μg/mL [Figs. 1, 9]. Previous studies in 2013 reported that a natural polyphenol compound found in *C. longa* inhibits the proliferation of various tumor cells, including breast cancer (Ponarulselvam et al., 2012). This statement supports the finding from the present study for anti-colon cancer activity of AgNPs synthesized using rhizome extracts of *C. longa* and *Z. officinale*. Other than medicinal plants, seaweed also studied for AgNPs synthesis with various biological applications. In a study by Balaraman et al. (2020), who synthesized AgNPs from seaweed *Sargassum myriocystum* aqueous extract and confirmed its anti-cancer activity.

4. Conclusion

In this study, synergistic aqueous extracts of rhizome of *C. longa* and *Z. officinale* have been used for the green synthesis of AgNPs. The spectral vibration of carboxyl (—C=O) and amine (N—H) groups in the *Z. officinale and C. longa* extracts might be involved in the synthesis of AgNPs. SEM results revealed that AgNPs are in a spherical shape with the size ranging from 42 to 61 nm, and from 20 to 51 nm by TEM analysis. MTT assay reveals that AgNPs had shown good anti-cancer activity against HT29 cells with the IC_{50} value of 150.8 μg/mL. Based on the study findings, it is concluded

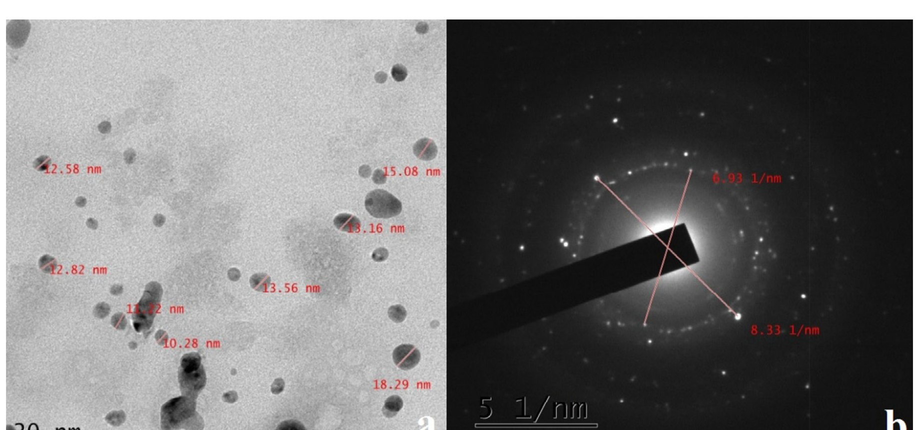

Fig 7. (a) TEM image of green synthesized AgNPs, and its SAED pattern (b) of green synthesized AgNPs.

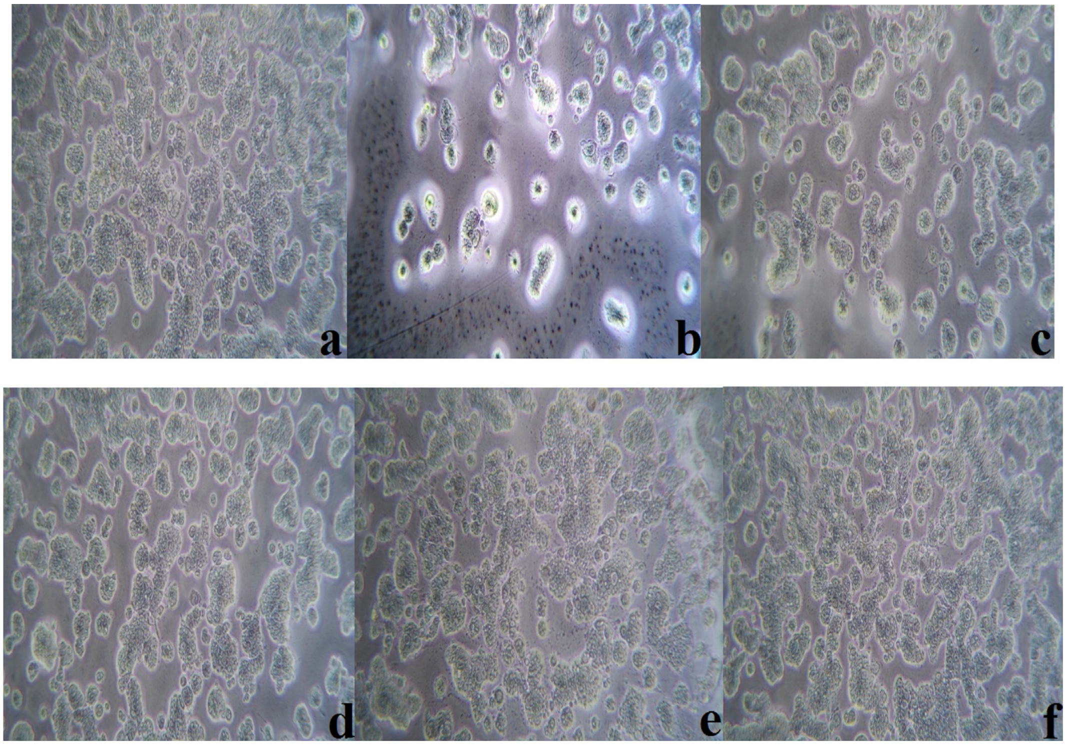

Fig 8. Anticancer activity of *Zingibe officinale and Curcuma longa* silver nanoparticles (a) control, (b)500 μg/mL, (c) 250 μg/mL, (d) 100 μg/mL, (e) 50 μg/mL and (f) 25 μg/mL.

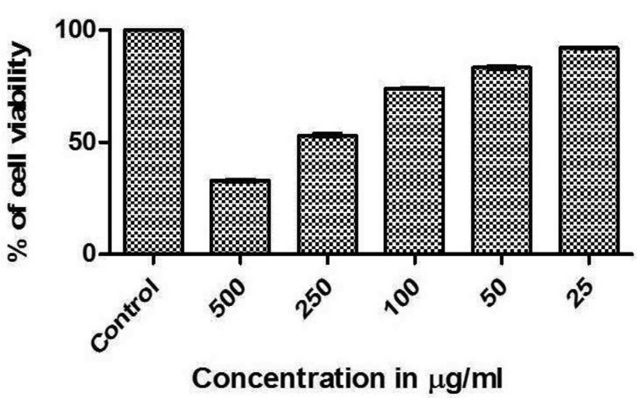

Fig 9. *In vitro* cytotoxicity effects of green synthesized AgNPs.

that AgNPs synthesized using rhizome of *Z. officinale and C. longa* have potential anti-cancer properties.

Declaration of Competing Interest

None declared.

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