Cancer Nanotechnology

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Artemisinin-loaded mesoporous silica nanoparticles/electrospun poly(lactic-co-glycolic acid) composite nanofibers for enhanced anticancer efficiency in breast cancer cells

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Abstract

Purpose: Antihyperglycemic drug artemisinin (Art) has recently gained attention as a potential anticancer treatment. In this study, the poly(lactic-co-glycolic acid) (PLGA) polymer was used to create Art-containing nanofibers (NFs) using the electrospinning technique.

Methods: The morphological characteristics, rate of degradation, and drug release profile of the NFs were described. In addition, we examined both the cytotoxic effects and internalization of reactive oxygen species (ROS), as well as the expression levels of apoptotic genes following the treatment of SK-BR-3 breast cancer cells with Art and Art-loaded PLGA nanofibers.

Results: The bead-free, smooth surface, and randomly aligned electrospun NFs released the medication quickly at first and then steadily for more than 2 weeks. They also showed a rather steady rate of deterioration over the course of 24 days. After 48h, SK-BR-3 cells exposed to ART-loaded NFs shown a substantial cytotoxicity compared to free Art. Additionally, Art-loaded NFs effectively increased intracellular ROS levels, inducing death in cancer cells. Gene expression studies further demonstrated the ability of the produced Art-loaded NFs to significantly modify Bax and Bcl-2 levels as well as activate caspases-3 and P53 compared to free Art.

Conclusion: Overall, the results demonstrated the Art-loaded PLGA nanofibers anticancer effectiveness, indicating that it may be employed as an implantable drug delivery system to decrease breast cancer recurrence following surgical resection.

Keywords: Artemisinin, Electrospinning, Nanofiber, PLGA, Breast cancer

Introduction

Cancer is one of the greatest challenging health problems in the world. The most general type of tumor among women is breast cancer (Pourgholi et al. 2021). The stage of the disease, the patient's medical history, and their general health all play a role in the current therapy of breast cancer (Alagheband et al. 2022). There are many types of cancer treatment strategies that can be used in cancer treatment, such as chemotherapy, radiation therapy, surgery, hormone therapy, targeted therapy, or a combination therapy (Wang et al. 2019). However, the emergence of new therapeutic approaches are limited because of the deficiency of substantial progress on survival rate and the metastatic tumors. Consequently, the search for new compounds with anti-tumor potential is crucial (Jafari-Gharabaghlou et al. 2023).

Phytochemicals are organic substances that are naturally present in plants and have been demonstrated to have positive impacts on human health, including anticancer capabilities. Polyphenols, flavonoids, and carotenoids are a few phytochemicals that may aid in the prevention of breast cancer (Hassani et al. 2022). Several studies have explored the potential benefits of phytochemicals for preventing and treating breast cancer (Altemimi et al. 2017).

Art is the phytochemical derivative of the Chinese herb *Artemisia annua* with antimalarial effects that are employed as the standard treatment for malaria (Efferth 2017). In addition to its anti-malarial properties, Art has demonstrated significant cytotoxic effects against various types of cancer and has shown promise as an anticancer agent. Art and its derivatives exhibit multiple biological actions in cancer cells (Wong et al. 2017) While Art exhibits certain limitations and disadvantages that restrict their biological functionality, these challenges are largely overcome by recent advancements in nanotechnology. Such limitations include short half-life, low solubility, poor bioavailability, limited stability in the bloodstream, and rapid metabolism and degradation. These improvements have significantly expanded the potential of Art for therapeutic applications, making them more viable and effective in clinical settings (Azar et al. 2022).

Poly(lactic-co-glycolic acid) (PLGA) and mesoporous silica nanoparticles (MSNs) are common materials used in the electrospinning process, a flexible method for creating nanofibers with a range of uses in industries like tissue engineering, drug delivery, and biomedical engineering (Batista et al. 2022). PLGA is a polymer matrix that is frequently utilized in electrospinning because of its superior processability and capacity to produce homogeneous nanofibers (Makadia and Siegel 2011). In tissue engineering, the electrospun PLGA fibers can act as scaffolds by offering structural support and encouraging the attachment and growth of cells. Furthermore, the body spontaneously metabolizes lactic acid and glycolic acid, the breakdown products of polylactic acid, which lowers the possibility of negative reactions (Xu et al. 2021).

MSNs are identified by their high surface area, variable pore diameters, and distinct porous structure (Ahmadi et al. 2023; Dadashpour et al. 2023). These characteristics make them perfect for uses where high therapeutic agent loading capacity and controlled release are required. Because of their enormous surface area, MSNs can be functionalized in a variety of ways for specialized uses such targeted medication administration, imaging, and catalysis (Jadhav et al. 2015). MSNs can be added to polymer matrices during electrospinning to improve the mechanical characteristics and usefulness of

the resultant nanofibers. Moreover, adding MSNs can increase bioactivity, enhance cell adhesion, and encourage tissue regeneration (Chen et al. 2019; Dadashpour et al. 2024). It is a very adaptable material for biomedical applications since the ratio of lactic acid to glycolic acid can be changed to change its rate of degradation.

A notable development in nanomaterials and biomedical engineering is the incorporation of mesoporous silica nanoparticles (MSNs) with poly (lactic-co-glycolic acid) (PLGA) during the electrospinning procedure (Chen et al. 2019). This novel method makes use of the special qualities of PLGA and MSNs to produce composite nanofibers that have improved functionality and may find use in a number of industries, most notably tissue engineering and drug delivery (Ding et al. 2019). The incorporation of MSNs into PLGA fibers offers a brand-new approach to developing extremely effective medication delivery systems (Rad et al. 2023). Due to their large surface area and adjustable pore diameters, MSNs have a substantial drug loading capacity and regulated release kinetics. These MSNs allow the construction of nanofibers that can encapsulate and release therapeutic substances over an extended length of time in a regulated manner when electrospun into PLGA fibers. Compared to traditional medication delivery methods, this strategy significantly improves drug delivery efficacy, decreases adverse effects, and lowers the frequency of administration (Vargason et al. 2021). In the current study, two-stage release of Art is investigated via the combination of mesoporous silica nanoparticles and PLGA nanofibers, with the aim of enhancing the anticancer efficacy of Art specifically in breast cancer cells.

Materials and methods

Materials

Art (purity > 99) was obtained from Sigma-Aldrich (St. Louis, USA). Cetyltrimethylammonium bromide (CTAB), tetraethoxysilane (TEOS), triethanolamine (TEA), ethanol (≥ 99.5%) and dimethyl sulfoxide (DMSO) were obtained from Merck Chemicals Company. Cell culture materials including 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide (MTT), DMEM, fetal bovine albumin (FBS), trypsin–EDTA, penicillin, and streptomycin were acquired from Nanchang Wante Technology Co., Ltd (Nanchang, China).

Preparation of MSNs

The synthesis of MSNs was done following the protocol of Ahmadi et al. (Ahmadi et al. 2023). Briefly, 0.5 g of CTAB, 0.08 g TEA and 20 mL DI water were placed on a magnetic stirrer hot plate at 80 °C for 2 h. Next, 2 mL TEOS, as the silica precursor was quickly added and stirred for 2 h until the formation of a white precipitate. The white powder was centrifuged and washed with using double distilled water and ethanol three times and dried under vacuum to obtain MSNs. A detailed schematic of the material preparation process is shown in Fig. 1.

Preparing and characterizing Art@MSNs

As reported by Dadashpour et al., Art was encapsulated in MSN with a slight modification (Dadashpour et al. 2023). At first, MSN (40 mg) and Art (100 mg) were added to the ethanol:acetone mixture (10 mL 70:30 v/v). After that, the reaction mixture was

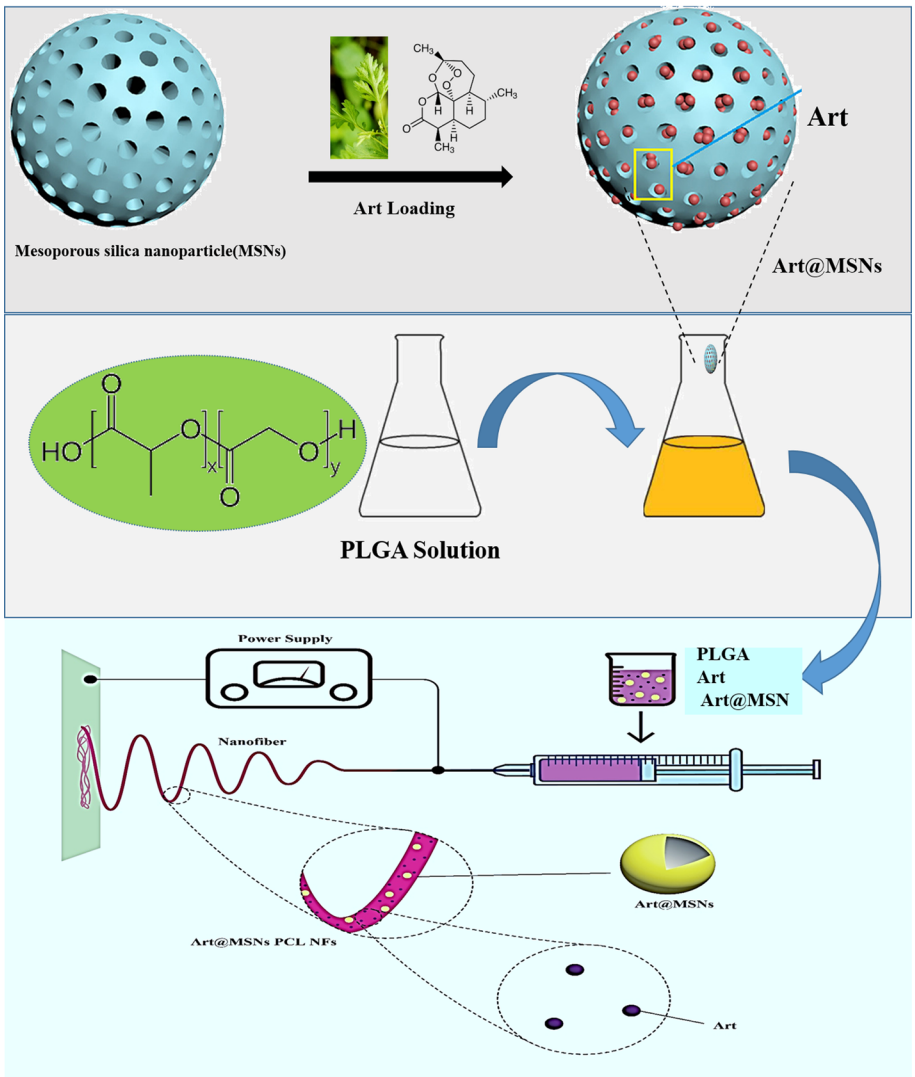

Fig. 1 A detailed schematic of the material preparation process

shaken for 24 h at 37 °C. Following centrifugation for 30 min (8000 g), the precipitate was washed with ethanol, and dried for 8 h at 80 °C. MSNs were analyzed using field-emission scanning electron microscopy (FE-SEM) to investigate surface morphology and particle size. Furthermore, the particle size, zeta potential, and hydrodynamic size distributions were measured at 25°C utilizing the Zetasizer Nano instrument (Malvern, UK).

Fourier transform infrared (FT-IR) spectroscopy was utilized to determine the characteristic functional groups of Art and Art-loaded MSN. Analyses of the samples were carried out in the infrared range of 400 to 4000 cm^{-1} using KBr pellets.

Fiber preparation and characterization

A horizontal electrospinning apparatus (Fanavaran Nanomeghias, Iran) was applied to synthesize the nanofibrous scaffolds based on our preceding studies (Firouzi Amandi

et al. 2023). Fabrication of NFs, including neat NFs, Art-PLGA NFs and Art@MSNs-PLGA NFs, was done using the electrospinning technique. An electrospinnable solution (at a concentration of 20% (w/v) was produced by adding PLGA (MW 35–45 kDa) in dichloromethane and methanol (4:1, v/v)0.15% wt of Art was transferred to the PLGA solution and magnetically stirred at 25 °C overnight to prepare the Art-encapsulated PLGA solution. Then, the solutions were electrospun into NFs at a constant flow rate of 0.5 mL h-1 with a distance of 20 cm between an aluminum foil-wrapped collector and a 22-gauge needle-equipped plastic syringe at the applied voltage of 20 kV. The fabricated NFs were vacuum dried at 50 °C overnight to eliminate the residual solvent before further use.

In order to observe the morphological features of the nanofibers, field-emission scanning electron microscopy (FE-SEM) was employed, using a MIRA3 TESCAN instrument from the Czech Republic with an accelerating voltage of 10 kV. FE-SEM images were analyzed with Image J software (National Institutes of Health, Bethesda, VA) to determine the mean diameter of nanofiber mats.

FT-IR spectroscopy was used to analyze the chemical configuration of the fibers within the range of 400–4000 cm^{-1}.

Loading rate and encapsulation efficiency

The loading and encapsulation efficiency of Art in MSNs were determined using UV–visible spectrophotometry at a wavelength of 420 nm. After the co-precipitation synthesis of Art-loaded MSN, the reaction mixture was centrifuged at 11,000 rpm for 10 min to separate unbound Art. The pellet was then dissolved in ethanol using sonication for 10 min to determine the percentage of Art in MSNs. Art loading efficiency was assessed according to Eq. (1, 2):

$$\text{Encapsulation efficiency (EE\%)} = \frac{\left(\text{Weight } of \text{ } applied \text{ } Art - \text{ weight } of \text{ } nonadsorbed \text{ } Art\right)}{\text{Weight } of \text{ } applied \text{ } Art} \times 100, \quad (1)$$

$$\text{Loading capacity (LC\%)} = \frac{\left(\text{Weight } of \text{ } applied \text{ } Art - \text{ weight of } nonadsorbed \text{ } Art\right)}{\text{Weight } of \text{ } MSNs} \times 100. \quad (2)$$

All measurements were made in triplicate and the average value was reported.

In vitro drug release studies

A dialysis method was implemented to assess the release behavior of Art from nanoparticles under different pH conditions. In this study, 20 mg of Art-loaded MSNs-PLGA nanofibers (Art@MSNs-PLGA NFs) were added to 3 mL of PBS at 7.4, and then sealed in a dialysis bag made of cellulose membrane with a molecular weight cut-off of 12,400 (Sigma-Aldrich). Dialysis bags were immersed under magnetic stirring in 38 mL of different pH solution at 25 °C under sinking conditions. At certain incubation time points, the concentration of Art was determined by pipetting 1 mL of the exterior buffer solution and measuring the amount of Art released using a UV–visible spectrophotometer

at a wavelength of 420 nm. The release of Art from Art-loaded MSN-NH_2 was evaluated by comparing the mean differences in absorbance between the suspension and pure Art.

Cell culture study

We obtained human breast cancer cells from the National Cell Bank of Iran (NCBI; Pasteur Institute, Tehran, Iran) and cultured those at 37 °C in a humidified atmosphere containing 5% CO_2 using DMEM medium supplemented with 10% fetal bovine serum (FBS) and 100-IU penicillin/ml, 100 µl streptomycin/ml. Previously testing the cytotoxic effects of samples, it was confirmed that the cells attained at least 80% confluency in well plates. This confirms a consistent and optimal cell population for perfect outcomes.

In vitro cytotoxicity studies—MTT assay

As a growing phase, SK-BR-3 cells were seeded into 96-well plates in DMEM media mixed with 10% fetal bovine serum and 100 µg/mL antibiotic solution at a constant temperature of 37 ^{0}C under moist atmosphere and 5% CO_2.The cells were rinsed with 200 µL of PBS, then the cells were exposed with different type of samples and incubated for 24 h. After the treatment period, the medium was removed from the cells. The MTT solution (20 µL/mL, 5 mg/mL) was pipetted to each well after 24 h, followed by four hours of darkness incubation. After incubation period, the medium containing MTT was discarded from the cells and the formed crystals were dissolved with 100 µL of DMSO and thoroughly mixed. The ELISA microplate reader (ALLSHENG; AMR-100) was utilized for determination the absorbance of each well at a wavelength of 570 nm.

Quantitative real-time PCR

According to manufacturer's instructions, TRIzol reagent (Life Technologies, USA) was employed to extract total RNA from cell samples. The quantity and quality of the isolated RNA samples were analyzed using a Nanodrop 8000 spectrophotometer. Reverse transcription was carried out using the SinaClon First Strand cDNA synthesis kit (SinaClone, Tehran, Iran) to obtain complementary DNA (cDNA). 1 µL of cDNA template (1000 ng), 10 µL of 2X Real-Time PCR Master Mix (High ROX; BioFACT, Korea), 8 µL of ddH2O, and 1 µL of each forward and reverse primer (5 µM) was employed for each 20-µL PCR reaction. The PCR assays were conducted at 95 °C for 10 min after enzyme activation. Then, 45 cycles were performed at 94°C for 10 s, 62°C for 30 s, and 72°C for 20 s. A housekeeping gene 18s rRNA was used to normalize the expression values. In order to create melting curves, the fluorescence of the SYBR green signal was monitored between 65 and 95°C. A twofold (bi-Ct) method was used in the analysis of the Q-PCR data, and each reaction was repeated in triplicate. For each run, no template control and no reverse transcriptase control were carried out.

Statistical analysis

The results are expressed as the mean ± standard deviation (SD). In order to perform the statistical analyses, Prism®7 software (GraphPad Software Inc., La Jolla, CA) was

used. An analysis of variance (ANOVA) or Student's t-test and Tukey's post-test were used to analyze the data. Statistical significance was defined as a p-value of 0.05. The experiments were repeated at least three times independently.

Results

Art@MSNs characterization

FT-IR analysis was done for Art, MSNs, Art@MSNs and Art@MSNs loaded nanofiber (Fig. 2 A-D). The band at 505 cm^{-1} MSNs and 813 cm^{-1} Art specifies the C–C bond. The peak at 1112 cm^{-1} Art@MSNs and 1282 cm^{-1} Art is because of the C–O bond. Other peaks at 1471 cm^{-1} Art@MSNs and 1512 cm^{-1} Art are due to C=C bond. The sharp peak at 2359 cm^{-1} is due to C=O bond present in pure Art. All these bands formation is possible due to the presence of carbon, oxygen and hydrogen present in the photochemical of natural components mainly Art. As a result, MSNs helps in the water solubility ability of Art@MSNs which helps in fast drug delivery.

Surface morphology of prepared MSNs and Art@MSNs was observed by SEM which observed that NPs are spherical shape. Micrograph of synthesized Art@MSNs is presented in Fig. 3a seen that average particle size of Art@MSNs is near 100 nm. Results of DLS presented that MSNs have uniform dispersion with an average size of 108 ± 0.21 nm, zeta potential (ZP) of -14.3 ± 2.8 mV, and a polydispersity index (PI) of 0.113. Additionally, it is found that Art@MSNs presented an average size of 120 ± 2.5

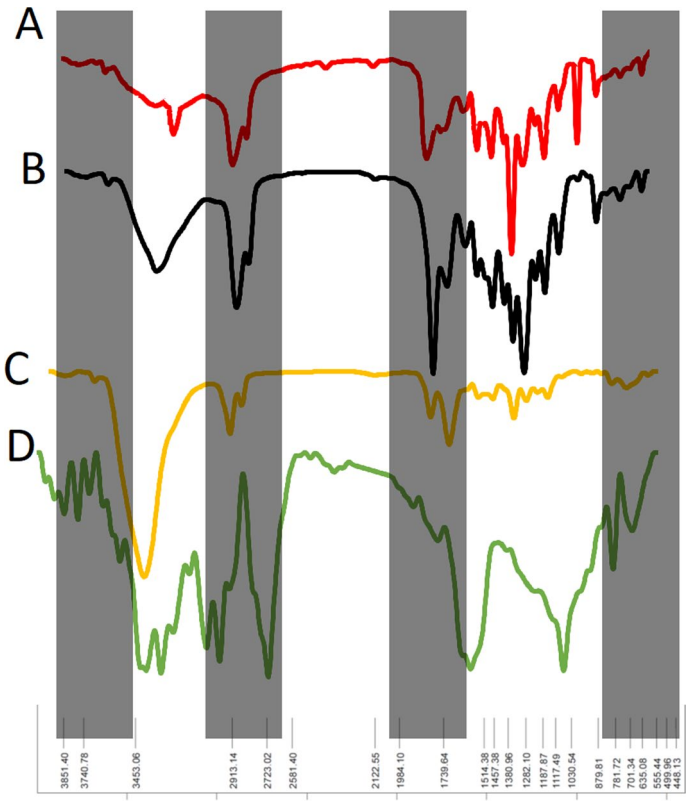

Fig. 2 FT-IR spectrum for Art (**A**), Art-NFs (**B**), MSNs-NFs (**c**) and Art@MSNs-NFs (**d**)

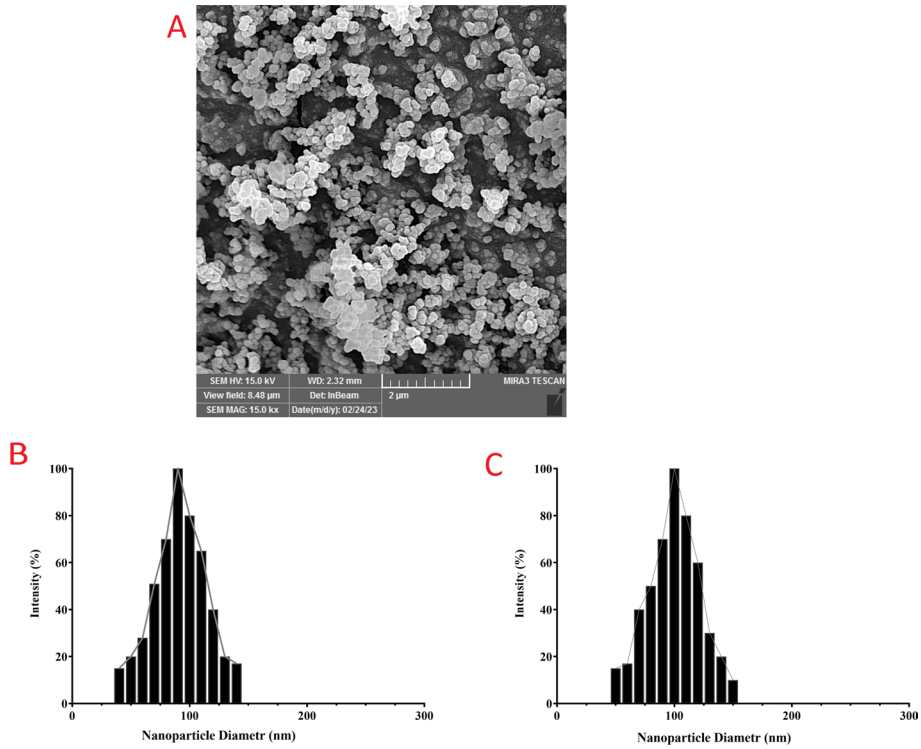

Fig. 3 Characterization of the prepared MSNs. FE-SEM image of Art@MSNs (**a**). The DLS analysis on mean diameter of Art@MSNs (**b** and **c**). Results are mean ± SD (n = 3)

nm, ZP of 2.9 ± 1.7mV, and PI of 0.151 (Fig. 3b,c. According to the FE-SEM and result, the MSNs were spherical particles with smooth surface (Fig. 3a).

UV–vis spectroscopy and Eq. (1–2) were performed to evaluate Art encapsulation efficiency and loading capacity. Consequently, Art@MSNs are reported to have a drug loading content of 9.1 and an encapsulation efficacy of 40.9%.

Characterization of the fabricated NFs

PLGA copolymer was selected for the production of Art and Art@MSNs-loaded electrospun mats. SEM was implemented to investigate the surface morphologies of the fabricated samples. Figure 4 a-d represents the SEM graphs of neat NFs, Art-NFs, MSNs-NFs, Art@MSNs-NFs. The diameter of the nanofibers of samples were in the range of 150–200 nm. In the FE-SEM images of all the manufactured mats of nanofibers, a bead-free morphology with randomly oriented smooth fibers and a non-homogeneous diameter distribution was observed.

In vitro release of art from nanoparticles

To determine the discharge behavior of Art from Art@MSNs-PLGA NFs when exposed to pHs of 7.4, a dialysis membrane method was utilized, as shown in Fig. 5. The results of the 100 h release of Art from NFs at pH = 7.4 and temperature of 37°C in PBS are shown. The release of nano-encapsulated Art took place in two stages. In the first stage, a controlled release was performed for 6 h with an explosive release

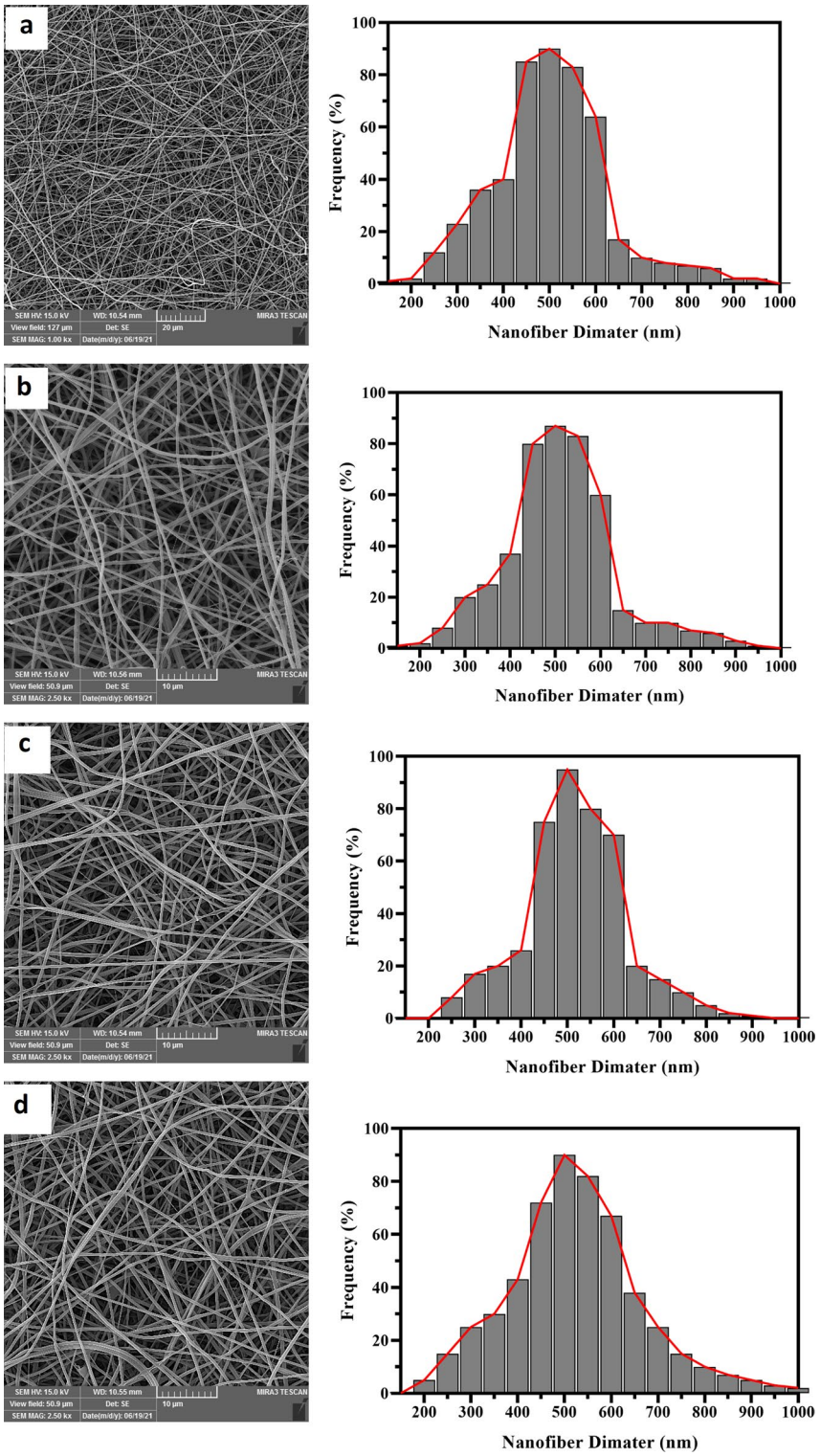

Fig. 4 Morphological features of the fabricated composite NFs. FE-SEM micrographs of neat NFs (**a**), Art-NFs (**b**), MSNs-NFs (**c**), Art@MSNs-NFs (**d**). These results are representative of $N = 3$ with similar outcomes

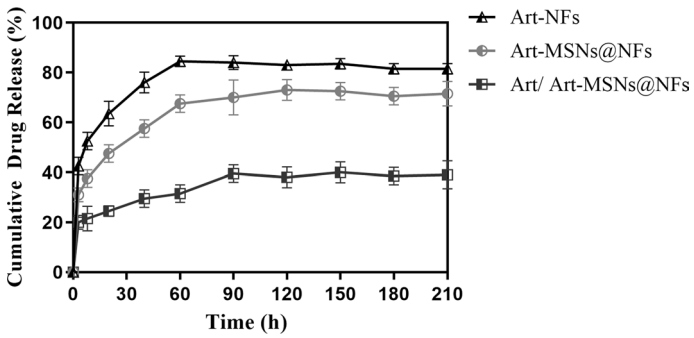

Fig. 5 Drug release patterns of Art from Art-NFs, Art@MSNs NFs, and Art/Art@MSNs-NFs. The data are presented as mean ± SD ($n = 3$)

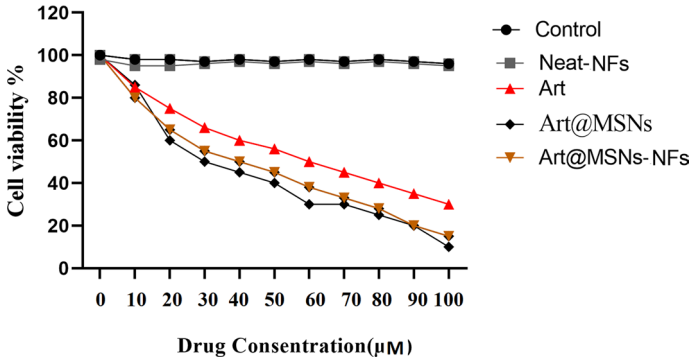

Fig. 6 Cell viability of SK-BR-3 human breast cancer cells after treatment by Art-NFs, Art@MSNs-NFs, and Art/Art@MSNs-NFs in 48 h. *$p \leq 05$ versus pristine Art was considered significant. The data are presented as mean ± SD ($n = 3$)

rate of the drug, which made it possible to release 25% of the trapped Art. The next step was a continuous phase of 90 h with a reduced and slow release rate, and the maximum release of Art from the MSN-loaded nanofiber reached 60% of the total drug, which showed that the persistence of Art in the MSN@NFs at pH 7.4 was confirmed. The highest explosive emission rate occurred in the first hour of the experiment at pH 7.4, and then the emission rate decreased. According to previous studies, it has been reported that high initial diffusion is due to the adhesion of nanoparticles to the surface of nanocarriers with loose bonds.

Cell viability assay

To assess the cytotoxicity of Art, Art@MSNs and Art@MSNs PLGA NX, the MTT assay was done using SK-BR-3 human breast cancer cells. Cells were treated at 10–100 μM concentrations for 48 h. The results show that cell viability reduced as a result of both forms in a time and dose-dependent manner, with Art@MSNs PLGA NFs exhibiting a greater cytotoxicity than free Art in all doses tested (Fig. 6). Data analysis of the IC_{50}s yielded from the 48 h MTT assays displayed that pure Art had an IC50 of 40/34 μM while Art@MSNs PLGA NFs had one of 55/22 μM.

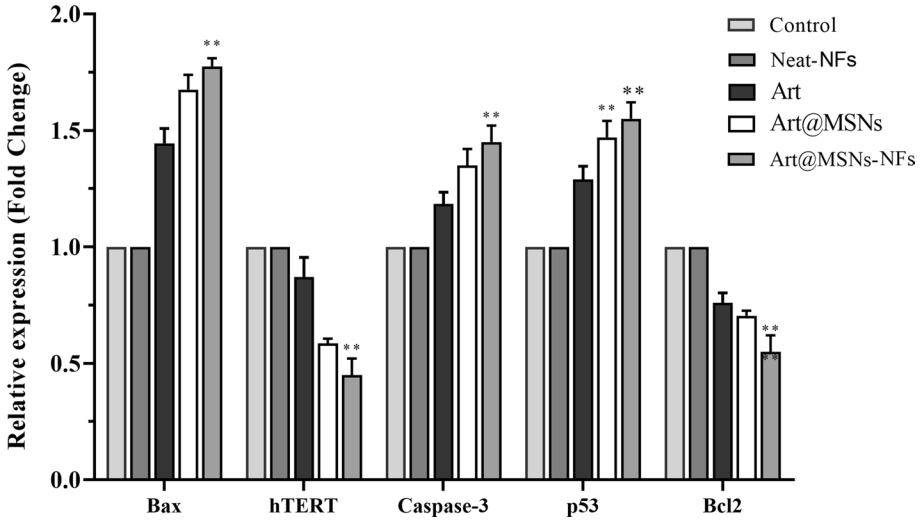

Fig. 7 Inhibitory effects of Art-NFs, Art@MSNsNFs, and Art/Art@MSNs-NFs on expression levels of caspase 3, p 53, hTERT, BAX and Bcl-2 in SK-BR-3 human breast cancer cells. *$P < 0.05$ and **$P < 0.01$ are the statistical differences between the combination form and individual drugs. Data represented are from three independent experiments. Results are mean ± SD ($n = 3$)

Quantitative reverse transcriptase-PCR (qRT-PCR)

To investigate the anticancer efficacy of Art and Art@MSNs-PLGA NFs, we conducted a quantitative assessment using real-time PCR on SK-BR-3 human breast cancer cells. The cells were treated with Art-PLGA NFs, Art@MSNs and Art@MSNs-PLGA NFs, focusing on the expression of genes associated with apoptosis. The results of the study showed that when Art was exposed to cells in its pure form and incorporated into MSNs@NFs, there was a decrease in hTERT, Bcl-2, p53 and caspase 3 and Bax gene expression while BAX gene expression increased (Fig. 7). These effects were further augmented when the drugs were loaded onto MSNs.

Discussion

An important field of this study focuses on targeted medication delivery for cancer therapy with the goal of enhancing cancer therapy efficacy while reducing adverse effects on healthy tissues. Silica-based porous materials are extensively utilized in drug delivery and biomedical applications, due to their ability to be modified in size, shape, and volume, as well as their surface properties (Tang et al. 2012). In comparison to other types of silica materials, mesoporous silica nanoparticles have been extensively investigated (Koohi Moftakhari Esfahani et al. 2022). Hydrogels and other formulations containing silica nanoparticles have been used for the past decade. They protect drug activity, promote biocompatibility, and provide controlled release profiles (Stephen et al. 2022).

Nanofiber scaffolds electrospun as drug delivery systems are regarded as a promising method of delivering anticancer drugs, especially in chemotherapy and localization following surgery. Electrospun nanofiber scaffolds are considered to be an attractive technique to cancer drug delivery because of their many attributes, including their ease of handling, better safety, and enhanced therapeutic efficacy (Kamalipooya et al. 2024). Various fabrication procedures for nanofibers consist of electrospinning, phase

separation, physical fabrication, and chemical fabrication. A variety of materials are employed to generate nanofibers according to their desired purposes, such as biodegradable polymers, artificial polymers, mesoporous, nonporous and hollow structures materials, core–shell systems, carbon, ceramic, metals, metal oxides materials, biocomponents, and multi-component materials. A nanofiber composite can significantly enhance the delivery of proteins, peptides, and growth factors. As a result, a nanofiber-based drug delivery system has tremendous potential, allowing them to be implemented in a variety of therapeutic fields (Huang et al. 2014; Feng et al. 2019; Shahhosseininia et al. 2018). Several biocompatible polymers have been employed to synthesize nanofibers using electrospinning, such as lactic co-glycolic acid (PLGA), poly butyl cyanoacrylate (PBCA), poly ethylene glycol (PEG), and poly(caprolactone) (PCL). In recent years, polymers with stimuli–responsive properties have been reported for the fabrication of polymeric scaffolds with biomedical applications (Mateti et al. 2021).

Additionally, colloidal nanoparticles have been electrospun into polymeric nanofibers for cancer treatments and drug delivery applications. Polymer nanofibers mimicking the extracellular matrix can suppress tumor cells and stimulate normal tissue regeneration after tumor resection (Tayebi-Khorrami et al. 2024). Drugs are often released from synthetic polymer fiber mats, such as polylactic-co-glycolic acid (PLGA) via degradation-controlled or diffusion-controlled mechanism. Despite the ability of these procedures to create multiple release profiles for fiber mats, these procedures still have some limitations, such as unwanted burst releases and toxic effects on healthy tissues (Al-Baadani et al. 2021).

Biocompatible and biodegradable PLGA nanofibers were engineered for biomedical applications including drug delivery and tissue engineering. Due to their considerable surface-area-to-volume ratio, fibers transport drugs more deeply, and because of their mucoadhesive properties, they provide a longer drug–mucosal retention period and improved drug dosage delivery to specific tissues, thereby reducing drug resistance and enhancing therapeutic efficiency (Pouroutzidou et al. 2022; Hemmati h et al. 2014; Mofarrah et al. 2023; Nejati et al. 2020).

Researchers have looked at the possibilities for using PLGA nanofibers and MSNs to deliver drugs. The development of dual drug release systems, which can release two distinct medications through two separate processes, has recently been the subject of study. The potential for two-staged drug release from MSNs and PLGA nanofibers has been very promising. While PLGA nanofibers are electrospun fibers that may be loaded with pharmaceuticals and released by diffusion or degradation, MSNs are porous materials with a large surface area and pore volume (Pouroutzidou et al. 2022). Using MSNs and PLGA nanofibers together can provide a two-staged drug release system.

In one report, electrospun composite nanofibers were shown to be effective in delivering drugs against breast cancer. In this work, curcumin (CUR) as natural anticancer agent was embedded into MSNs, and the CUR-loaded MSNs (CUR@MSNs) were then integrated into poly(lactic-co-glycolic acid) (PLGA) via a blending electrospinning process (CUR@MSNs/PLGA). Based on in vitro and in vivo results of this study, CUR@MSNs/PLGA NFs can effectively deliver CUR to breast cancer cells, resulting in significant anti-proliferative effects (Mohebian et al. 2021).

Another study developed novel nanofiber composites for burst and sustained CUR release. In this study, an electrospun composite nanofiber was prepared via encapsulation of free CUR and CUR-loaded MSN into a hybrid of gelatin and polycaprolactone (GEL/PCL) for a relatively prolonged release pattern of CUR. As a result of this study, composite nanofibers can function as a powerful implantable drug delivery system for postoperative breast cancer therapy due to their dual drug release mechanisms (Serati-Nouri et al. 2021).

By showing the possibility of combining mesoporous silica nanoparticles with PLGA nanofibers to boost the efficacy of Art, a natural substance with significant anticancer effects, the research advances our understanding of targeted medication delivery for the treatment of cancer. According to the study, loading Art in these materials can regulate and prolong medication release over time, increasing its effectiveness against breast cancer cells (Mitra et al. 2022).

The potential effects on upcoming cancer treatments are enormous. Cancer treatment may be revolutionized by targeted drug delivery systems that increase the effectiveness and safety of chemotherapy medications (Chehelgerdi et al. 2023). Targeted drug delivery systems can lessen the adverse effects of conventional chemotherapy, such as hair loss, nausea, and tiredness, by delivering medications directly to cancer cells. Furthermore, the creation of more potent and non-toxic cancer therapies may be facilitated by the utilization of natural substances like Art in targeted drug delivery systems. Targeted drug delivery systems may become a common component of cancer treatment as research in this field advances, enhancing patient results and quality of life (Hemmati h et al. 2014; Patra et al. 2018).

The immortalization of cancer cells is intrinsically linked to their ability to maintain telomere length through the upregulation of telomerase, a ribonucleoprotein complex composed of the catalytic subunit hTERT (human Telomerase Reverse Transcriptase) (Reddel and R, 2014). Several studies have demonstrated that breast cancer tissues exhibit significantly higher hTERT expression and/or telomerase activity compared to adjacent healthy tissues, underscoring the crucial role of telomere maintenance in the perpetuation of this malignancy. Consequently, a multifaceted approach targeting both the apoptosis regulatory genes, such as Bcl-2 and Bax, as well as the telomere maintenance mechanism, represented by hTERT, may prove to be a beneficial therapeutic strategy for the management of colorectal cancer (Firouzi Amandi et al. 2024).

The mitochondrial-mediated apoptosis pathway is a critical regulator of programmed cell death, and its dysregulation is a hallmark of various cancers. This pathway is primarily governed by the interplay between the anti-apoptotic protein Bcl-2 and the pro-apoptotic protein Bax, which have been extensively documented as fundamental to the persistence and proliferation of numerous malignant tumors. Accordingly, the modulation of these molecular players could potentially induce apoptosis in tumor cells, thereby impeding their progression (Nguyen et al. 2023).

The anticancer properties of Art have been investigated and documented in various types of cancer cells, including those affecting the breast, prostate, ovaries, cervix, and leukemia. These studies have been conducted both in vitro and in vivo (Zyad et al. 2018). It has been confirmed that Art prevents cell proliferation by promoting apoptosis in breast cancer cells. As a result, Art enhances the levels of reactive oxygen species

(ROS), resulting in oxidative stress, which can trigger the cytotoxicity of tumor cells (Greenshields et al. 2019). In the treatment of breast cancer, Art has also been discovered to have synergistic benefits when taken with other chemotherapeutic drugs, such as tamoxifen. The existing evidence shows that Art may be a viable therapeutic agent for breast cancer, even if additional study is still required to fully understand the processes underlying the drug's anticancer properties and its potential application in treating the illness (Jamalzadeh et al. 2017).

By highlighting strategies to improve the specificity and effectiveness of medicines, this research has advanced our understanding of targeted drug delivery for the treatment of cancer. Future cancer therapies might be significantly impacted by this discovery since direct medication delivery to cancer cells can lessen damaging effects on healthy tissues and side effects.

Conclusion

In current work, Art was delivered into SK-BR-3 cells using Art@MSNs-PLGA NFs. Because of their high loading capacity, biocompatibility, and controlled release characteristics, MSNs and PLGA nanofibers are used as drug delivery systems. As it permits the controlled release of many medications at various rates, this strategy offers a great deal of potential for enhancing drug delivery effectiveness and safety. It also offers a potential strategy for creating efficient and secure anticancer treatments. Our findings reveal that Art@MSNs-PLGA NFs, which promotes apoptosis, targets the viability and proliferation of SK-BR-3 cells more efficiently than free Art. This approach lays the groundwork for advancements in drug delivery, targeting and therapeutics. Incorporating Art into this framework opens new avenues for cutting-edge research in cancer biology and strategies to treat specific cancers. Generally, this study provides not only technical insights into the synthesis of MSNs and nanofibers, but also contributes to the evolving landscape of targeted drug delivery system and therapies. In conclusion, we hope that our research will provide the base for future clinical trials of Art-based nanoformulation therapy for breast cancer treatment and prevention in high-risk patients.

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Author contributions
MEV, ED, VV, SAS, AFA, ME, MH and ZM: investigation, methodology, data curation, preparation of original draft, writing—reviewing and editing. LR and MD: supervision, conceptualization, funding acquisition, reviewing and editing. All authors reviewed the manuscript.

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Declarations

Ethics approval and consent to participate
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Consent for publication
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Competing interests
The authors declare that they have no competing interests.

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