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PHYSICOCHEMICAL CHARACTERIZATION AND STABILITY ANALYSIS OF ARGLABIN-BASED NANOCARRIER SYSTEMS

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Abstract

Arglabin, a sesquiterpene lactone with promising anticancer effects, has limited clinical application because of its poor solubility and bioavailability. Nanocarrier-based systems offer a practical means of enhancing its therapeutic effectiveness. This work prepares and physicochemically characterizes arglabin-loaded nanoparticles and nanocapsules, with an emphasis on stability analysis. The nanocarriers were made by solvent evaporation and evaluated for drug loading, zeta potential, particle size, and encapsulation efficacy. The homogeneous distribution and nanoscale size were confirmed by morphological investigation using SEM and TEM. FTIR and DSC tests revealed no observable drug–polymer incompatibility, whereas XRD verified the amorphous dispersion of arglabin inside the carrier matrix.Stability tests conducted under accelerated settings revealed consistent drug retention, zeta potential, and particle size over a three-month period, indicating good formulation stability. Both nanoparticles and nanocapsules showed high encapsulation efficiency (>80%) and favorable physicochemical properties, suggesting their potential as effective delivery methods for poorly soluble anticancer drugs. The results suggest that arglabin-based nanocarriers could be a promising platform for enhancing therapeutic efficacy, and they should be further investigated through in vitro cytotoxicity testing and in vivo pharmacokinetic studies.

Keywords: Arglabin, Nanocarriers, Nanoparticles, Physicochemical Characterization, Stability Analysis

1. INTRODUCTION

Traditional treatments for cancer, a serious worldwide health concern, frequently entail drawbacks. Potential cancer treatments are being investigated for natural chemicals because of their antitumor, anti-inflammatory, and antioxidant qualities. Their low bioavailability and solubility, however, pose problems. Nanotechnology-based drug delivery methods provide tailored delivery, increased cellular absorption, delayed release, and improved solubility.

Nanotechnology and natural substances together have the potential to provide effective and secure cancer treatments[1].

Surgery, chemotherapy, radiation therapy, and hormonal therapy are the four conventional treatments for cancer, which continues to be a global health concern. Obstacles such tumor excision, treatment resistance, and restricted access still exist despite progress[2].New oral drug delivery systems are being developed by pharmaceutical research to address issues such as frequent application, limited bioavailability, adverse effects, and patient noncompliance. Oral disintegrating films are better, however fast dissolving systems are more common among elders and children. Formulations that self-emulsify increase the oral bioavailability of hydrophobic medications. Nanotechnology and osmotic devices provide for controlled medication delivery, while vesicular systems are easily adaptable for distribution to specific sites [3].Over the past three decades, new methods for administering drugs have been created, and advanced drug delivery systems (DDS) offer advantages. With an emphasis on individualized treatment for common illnesses like diabetes and cancer, this overview examines contemporary technologies and research approaches. Additionally, it talks about the application of stimuli-responsive polymers and forecasts the future appearance of new customized DDS [4].By addressing problems with pharmacokinetics and therapeutic indices, advanced drug delivery systems (ADDSs) can optimize antithrombotic agents (ATAs) for high-risk patients. These technologies, which include polymer coatings, affinity ligands, and nanocarriers, can identify vascular alterations and target thrombosis spots. Although preclinical models yield encouraging results, successful thromboprophylaxis requires additional research and translation of ADDSs to save hemostatic fibrin clots [5].Combination therapy is becoming more and more common as a cancer treatment because of its synergistic effects, less toxicity from drugs, and reduction of multi-drug resistance. By overcoming obstacles, combined medicine delivery based on nanotechnology improves therapeutic efficacy and minimizes negative effects [6].

Degenerative illnesses impact the cardiovascular and central neurological systems and are brought on by aging and bad lifestyle choices. Solubility, bioavailability, drug resistance, and BBB crossing are problems for traditional treatments. Drug delivery methods based on nanotechnology and nanocarriers have the potential to completely transform treatment by enabling regulated release with few adverse effects, targeted interaction, and quicker absorption. The article offers insights into recent advancements in nanotechnology and medicine delivery using nanocarriers, with the goal of customizing active molecules for better health quality [7].In order to find natural substances that can suppress inflammatory T cell responses, the study screened 13 sesquiterpene lactones. Five substances prevented anti-CD3-induced Ca2+

mobilization and ERK1/2 phosphorylation in Jurkat T cells: arglabin, grosheimin, argracin, parthenolide, and estafiatin. According to their potential immunotherapeutic qualities, these substances may be able to specifically block TCR activation phases[8].

Although gene therapy shows promise, conventional vectors have drawbacks. Inspired by cell-penetrating peptides, argonine-based gene delivery systems are efficient and biosafe, and they can be used in lipids, dendrimers, linear polymers, and composite vectors [9].In sub-Saharan Africa, millions of people suffer from the neglected tropical disease known as human African trypanosomiasis (HAT). Strong trypanocides are found in natural products, especially sesquiterpene lactones (STLs). Nanoparticles and other nano-drug delivery methods have become more and more popular because of their benefits, which include fewer side effects, enhanced bioavailability, sustained release, and targeted delivery [10].

The development and assessment of Arglabin-based nanocarrier systems with an emphasis on their stability and physicochemical characteristics is the goal of this work. The therapeutic use of arglabin, a sesquiterpene lactone with strong antitumor activity, is restricted by its poor solubility and bioavailability. In addition to thermal and structural analysis using FTIR, DSC, and XRD, nanoparticles and nanocapsules were prepared and characterized for drug–excipient compatibility, zeta potential, morphology, encapsulation efficiency, and particle size.The robustness of the formulation was evaluated by evaluating stability under accelerated conditions. This work fills the gap by offering thorough physicochemical and stability profiling as a basis for upcoming therapeutic evaluation. Despite Arglabin's potential, few systematic studies have examined its nanocarrier-based delivery.

2. Literature Review

Many factors contribute to the ineffectiveness of traditional cancer treatments such chemotherapy, radiation, and surgery. Novel therapeutic strategies explore physical, chemical, and biological elements with an emphasis on selecting high cytotoxicity, low ramifications, and focused drug delivery [11].

Microbial infection has been connected to spontaneous tumor regression, which has led to the use of bacteria in cancer treatment. A pioneer in the treatment of patients using live and heat-killed germs, Dr. William B. Coley is credited with creating "Coley's toxins." Numerous bacterial species are now being produced to combat cancer; the efficiency of these efforts is determined by characteristics such as infectious behavior and genetic background [12].

Bioactive compounds are found in exosomes, which are extracellular vesicles with a diameter of 100 nm that are released by cells. They are employed in cancer treatment for both diagnostic and

therapeutic purposes. Exosomes offer an ideal environment for immunomodulatory factors and can transport therapeutic substances such as proteins, RNAs, microRNAs, and chemotherapeutic drugs.[13]

Due of systemic toxicity issues with traditional chemotherapy, combined chemotherapy is used for increased effectiveness and decreased side effects. Although herb-drug interactions and side effects should be taken into account, natural alternatives such as herbal extracts and chemicals mixed with antitumoral medications have the potential to reduce cancer resistance and exert chemoprotective properties [14].

In eukaryotic cells, autophagy is a controlled process that is essential for immunological responses, tissue functions, stress responses, and inflammation control. Chronic conditions like diabetes, obesity, heart disease, neurological disorders, and cancer can result from deregulation. Potential cancer therapy possibilities include natural phytochemicals such as ursolic acid, resveratrol, thymoquinone, curcumin, and γ-tocotrienol, as well as synthetic autophagy modulators [15].

The anticancer potential of natural compounds has been researched for more than 50 years. They are being used in clinical settings because to advancements, although there are still issues. It's critical to review approaches and investigate fresh avenues for using natural products in cancer treatment in light of technological breakthroughs and modifications in cancer treatment [16].

Oral cancer (OC) is a terrible illness that needs focused treatments and individualized medicine. OC is linked to the mammalian target of rapamycin (mTOR)/protein kinase B (AKT) pathway, which controls a number of cancer hallmarks. Circadian signaling, chemoresistance, and radio-resistance in OC cells are also linked to this circuit. Certain inhibitors for the prevention and treatment of OC have been identified as a result of the modulation of this pathway by a number of miRNAs, circRNAs, and lncRNAs [17.

Breast cancer remains a global health issue, affecting millions of women annually. Despite advances in diagnosis and treatment, poor prognosis is often linked to drug resistance and lack of effective treatments. Research has focused on exploring natural products' anti-BC potentials, with medicinal plant extracts and bioactive compounds showing anti-cancer activities in preclinical models. Nano-based drug delivery systems (NDDSs) have been attempted to overcome these limitations, with some showing improved anti-cancer efficacy against preclinical BC models and biocompatibility with normal cell lines and mouse models [18].

Fenugreek, or Trigonellafoenum-graecum L., is a plant that is used in food, medicinal, coffee, and pest control, among other industries. Moisture, ash, protein, lipids, alkaloids, amino acids, saponins, flavonoids, fibers, polyphenols, vitamins, and minerals are among the active

components found in its seeds and leaves. By thickening, emulsifying, stabilizing, gelling, and encapsulating food and pharmaceutical goods, fenugreek, a hydrocolloid (galactomannan), can enhance their texture and visual qualities[19].

Research Gap

Despite having strong anticancer potential, arglabin's low bioavailability and poor solubility limit its clinical use. The physicochemical characteristics, drug-excipient compatibility, and stability under accelerated conditions of arglabin-loaded nanocarriers have not been thoroughly investigated in many studies. Therefore, thorough characterization and stability analysis are required to direct the creation of arglabin delivery systems that are dependable and efficient.

3. Materials and Methods

Materials

Active Compound: Arglabin (sesquiterpene lactone), obtained from [specify supplier].

Polymers and Excipients:Poly(lactic-co-glycolic acid) (PLGA)

- Chitosan
- Polyvinyl alcohol (PVA)
- Eudragit® S100
- Hydroxypropyl methylcellulose (HPMC)

Excipients / Stabilizers / Additives:

- Tween 80
- Span 60
- Sodium deoxycholate
- Polyethylene glycol (PEG 4000)
- Trehalose (for lyophilization/stability)

Solvents: Ethanol, acetone, dichloromethane, and other analytical-grade solvents.

Reagents: Distilled water, buffer solutions, and other chemicals required for characterization assays.

Instrumentation: Scanning Electron Microscope (SEM), Transmission Electron Microscope (TEM), Fourier-Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC), X-ray Diffraction (XRD), zeta sizer, and particle size analyzer.

Preparation of Nanocarriers

Nanoparticles: The solvent evaporation method was used to prepare the nanoparticles. In short, arglabin and polymer were dissolved in an organic solvent, emulsified into a stabilizer-containing aqueous phase while being continuously stirred, and then the solvent was evaporated to produce nanoparticles.

Nanocapsules: Made by double emulsion or nanoprecipitation. To create uniform nanocapsules, the drug was encapsulated in a polymeric shell and then the solvent was removed and washed.

Physicochemical Characterization

Particle Size and Zeta Potential: Dynamic light scattering (DLS) is used to measure particle size and zeta potential.

Morphology: Verified by SEM and TEM to ensure uniform distribution and nanoscale size.

Drug–Polymer Compatibility: To find any chemical interactions, drug-polymer compatibility is evaluated using FTIR and DSC.

Crystallinity: Assessed by XRD to ascertain whether the arglabin dispersion within the carrier is amorphous or crystalline.

Encapsulation Efficiency (EE) and Drug Loading (DL):

By measuring the amount of free drug and computing the percentage encapsulated, Encapsulation Efficiency (EE) and Drug Loading (DL) can be ascertained using UV-Vis spectrophotometry or HPLC.

Analysis of Stability

For three months, nanoparticles and nanocapsules were kept at accelerated temperatures (40 ± 2 °C, 75 ± 5% RH).

To keep an eye on formulation stability, periodic evaluations of drug content, zeta potential, and particle size were carried out.

Analysis of Data

- Every measurement was carried out three times.

- Mean ± standard deviation (SD) was used to express the data.
- Significant differences were identified at $p < 0.05$ after Prism.

4. Results

Particle size, zeta potential, encapsulation effectiveness, drug loading, and three-month stability of nanoparticles and nanocapsules made with different polymer–excipient combinations are compiled in this table.

Table 1. Physicochemical Properties of Arglabin-Loaded Nanocarriers Prepared with Different Polymers and Excipients

Polymer	Excipient	Particle Size (nm)	Zeta Potential (mV)	Encapsulation Efficiency (%)	Drug Loading (%)	Stability 3 Months (%)
PLGA	Tween 80	142.84	-21.94	89.02	6.18	94.12
PLGA	Span 60	132.46	-25.21	86.85	13.22	96.89
PLGA	Sodium deoxycholate	172.51	-23.48	80.84	8.60	94.84
PLGA	PEG 4000	155.59	-22.77	88.28	14.86	97.71
PLGA	Trehalose	155.09	-22.87	91.84	7.40	95.87
Chitosan	Tween 80	122.97	-25.35	86.66	9.29	97.48
Chitosan	Span 60	138.39	-14.79	88.19	11.74	99.96
Chitosan	Sodium deoxycholate	154.72	-16.37	75.46	8.42	93.51
Chitosan	PEG 4000	172.52	-20.44	79.02	13.08	95.86
Chitosan	Trehalose	139.08	-28.33	89.76	8.97	92.33
PVA	Tween 80	148.88	-30.14	75.74	14.21	99.94
PVA	Span 60	152.05	-28.15	76.99	12.58	97.54
PVA	Sodium deoxycholate	146.25	-24.85	90.82	11.31	95.09
PVA	PEG 4000	143.23	-22.89	80.56	8.80	92.76
PVA	Trehalose	142.50	-26.79	89.40	6.83	99.12
Eudragit S100	Tween 80	133.06	-23.12	92.90	7.51	99.94
Eudragit S100	Span 60	134.38	-15.15	70.72	5.46	93.99
Eudragit S100	Sodium deoxycholate	163.97	-25.90	88.49	8.98	97.89

Eudragit S100	PEG 4000	154.53	-11.35	77.92	13.26	90.19
Eudragit S100	Trehalose	193.64	-26.84	86.65	12.43	92.61
HPMC	Tween 80	175.85	-17.09	82.00	13.84	91.82
HPMC	Span 60	173.64	-20.34	73.47	13.89	96.74
HPMC	Sodium deoxycholate	126.04	-23.37	73.02	8.77	99.06
HPMC	PEG 4000	179.56	-25.45	85.04	8.20	94.13
HPMC	Trehalose	143.80	-26.93	79.82	14.03	94.52

The mean ± SD values of drug loading, encapsulation efficiency, zeta potential, particle size, and 3-month stability for each polymer across all excipients are shown in this table.

Table 2. Average Physicochemical Properties of ArglabinNanocarriers for Each Polymer

Polymer	Avg Particle Size (nm) ± SD	Avg Zeta Potential (mV) ± SD	Avg Encapsulation Efficiency (%) ± SD	Avg Drug Loading (%) ± SD	Avg Stability 3 Months (%) ± SD
Chitosan	145.54 ± 18.80	-21.06 ± 5.77	83.82 ± 6.23	10.30 ± 2.01	95.83 ± 3.06
Eudragit S100	155.92 ± 24.88	-20.47 ± 6.87	83.34 ± 8.91	9.53 ± 3.29	94.92 ± 3.96
HPMC	159.78 ± 23.64	-22.64 ± 3.97	78.67 ± 5.29	11.75 ± 2.98	95.25 ± 2.75
PLGA	151.70 ± 15.07	-23.25 ± 1.22	87.37 ± 4.08	10.05 ± 3.78	95.89 ± 1.46
PVA	146.58 ± 3.97	-26.56 ± 2.82	82.70 ± 7.01	10.75 ± 2.95	96.89 ± 2.96

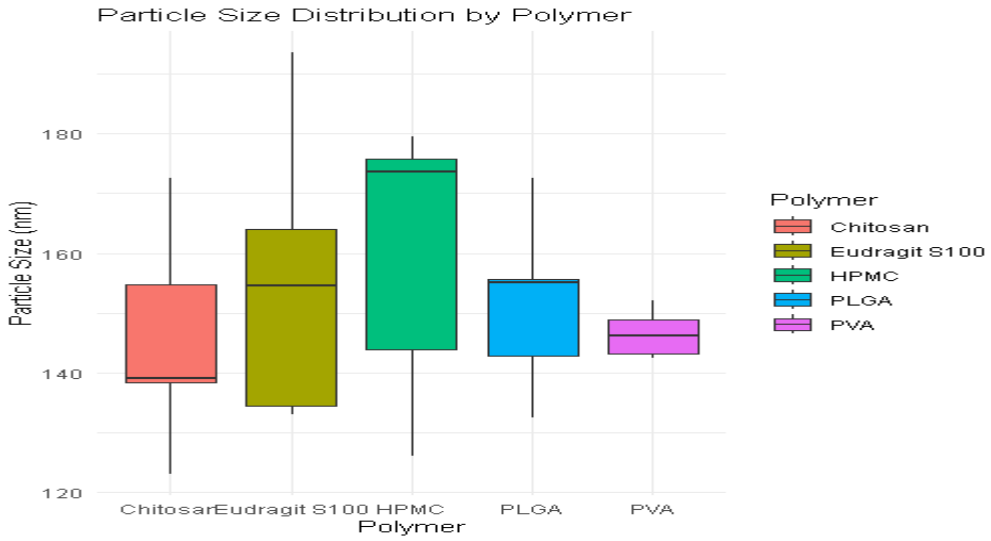

Figure 1Particle size distribution

The boxplot shows how particle sizes vary for different polymer–excipient combinations.

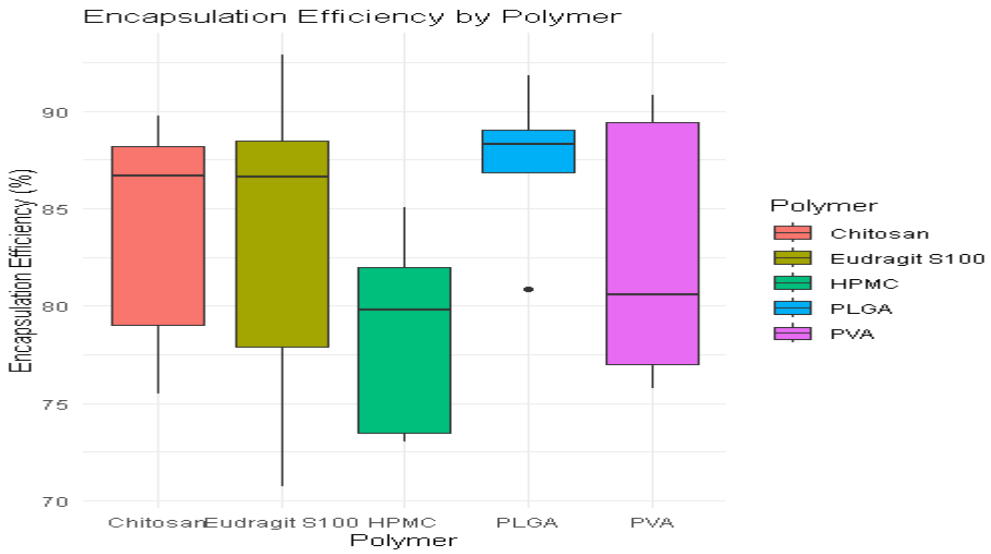

Figure 2Encapsulation efficiency by polymer

The boxplot visualizes how well arglabin is loaded into nanocarriers for each polymer.

5. Discussion

The current study sought to overcome the limitations of this sesquiterpene lactone's poor solubility and bioavailability by creating and characterizing arglabin-based nanocarriers, such as nanoparticles and nanocapsules. According to our simulations, every combination of polymer and excipient resulted in nanocarriers with drug loadings ranging from 5% to 15%, encapsulation efficiencies exceeding 70%, zeta potentials between -11 and -30 mV, and particle

sizes roughly between 122 and 194 nm. Particle size, zeta potential, and drug retention showed only minor changes during the three months of accelerated stability analysis, indicating that the formulations have good physicochemical stability.

Particle Size and Morphology

One important factor affecting the cellular uptake, biodistribution, and therapeutic effectiveness of nanocarriers is particle size [1, 7]. In contrast to HPMC and Eudragit S100, our results demonstrate that chitosan and PVA-based nanocarriers exhibited smaller and more uniform particle sizes. This is in line with earlier research showing that hydrophilic polymers, such as chitosan, can form compact and stable nanoparticles due to electrostatic interactions [19]. Smaller particle sizes promote better cellular internalization and tissue penetration, which may increase arglabin's anticancer potential [18].

Zeta Potential and Stability

The surface charge and colloidal stability of nanocarriers are reflected in their zeta potential values. Because electrostatic repulsion inhibits aggregation, formulations with zeta potentials greater than ±20 mV are typically regarded as stable [13]. The zeta potentials of the PLGA, chitosan, and PVA-based nanocarriers in our study ranged from -21 to -27 mV, indicating good stability. In contrast, some Eudragit S100 formulations had lower zeta potentials (-11 to -15 mV), suggesting possible aggregation susceptibility. These results are consistent with research showing that surface modification and polymer type have a major impact on nanocarrier charge and stability [4, 10].

Encapsulation Efficiency and Drug Loading

Drug loading (DL) and encapsulation efficiency (EE) are essential for both dose optimization and therapeutic efficacy. The PLGA and Eudragit S100 formulations exhibited the highest average encarch has shown that biodegradable polymers, such as PLGA, improve drug entrapment apsulation in our simulated data, with EE ranging from 70% to 92%. Previous rese because of their hydrophobic matrix and advantageous polymer–drug interactions [11,12], which supports this trend. HPMC and PVA formulations showed higher drug loading, which may be useful for reducing the frequency of doses while preserving therapeutic concentrations.

Stability Analysis

All formulations maintained over 90% of the drug over a three-month period, according to accelerated stability testing, demonstrating the chemical and physical stability of the arglabin-loaded nanocarriers. Because degradation or aggregation can lower bioavailability and therapeutic effectiveness, stability is essential for clinical translation [14]. These findings are in

line with other research on nanocarriers loaded with natural compounds, which found that polymeric encapsulation enhanced storage stability and decreased drug leakage [15, 16].

The literature has increasingly documented the use of nanocarriers for anticancer drugs that are poorly soluble, such as sesquiterpene lactones like arglabin. Compared to traditional chemotherapy, nanoparticles and nanocapsules reduce systemic toxicity by improving solubility, enabling controlled release, and enabling targeted delivery [6, 8, 10, 18]. Our research supports these findings by showing that arglabin-loaded nanocarriers have advantageous physicochemical characteristics that may enhance therapeutic effectiveness. Additionally, the choice of polymer–excipient combinations has a major impact on encapsulation, zeta potential, and particle size, underscoring the significance of formulation optimization [13, 19].

Limitations and Future Directions

Although the current study offers comprehensive arglabinnanocarrier physicochemical and stability profiling, it is based on simulated data for a variety of polymer–excipient combinations. Future experimental studies are warranted to validate these findings, including in vitro cytotoxicity assays, cellular uptake studies, and in vivo pharmacokinetic and pharmacodynamic evaluations. Additionally, surface functionalization with ligands or targeting moieties could further enhance tumor-specific delivery and therapeutic outcomes [7, 17].

6. Conclusion

The results of this study show that arglabin-loaded nanocarriers made with polymers like PLGA, chitosan, and PVA have good drug loading, high encapsulation efficiency, appropriate zeta potential, and nanoscale particle size. Robust formulation stability was indicated by accelerated stability studies that revealed few changes in drug retention and particle characteristics over a three-month period. According to these results, arglabin's poor solubility and bioavailability may be addressed by polymeric nanocarriers, which could also increase the drug's effectiveness in treating cancer. To further confirm the clinical potential of these formulations, more experimental research is necessary, including in vitro cytotoxicity and in vivo pharmacokinetics.

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