

INTRAVENOUS ADMINISTRATION OF LIPOSOMAL THYMOQUINONE FOR THE TREATMENT OF TRIPLE-NEGATIVE BREAST CANCER: A NOVEL THERAPEUTIC STRATEGY

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Abstract : Triple-negative breast cancer (TNBC) remains one of the most challenging subtypes of breast cancer to treat due to the absence of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2), which limits the applicability of targeted hormonal therapies. Conventional chemotherapies are associated with poor selectivity and severe systemic side effects, underlining the urgent need for more effective and safer alternatives. Thymoquinone (TQ), a natural compound derived from *Nigella sativa*, has shown promising anticancer activity, including apoptosis induction, anti-proliferative effects, and inhibition of metastasis in various cancer models. However, its clinical translation is hindered by poor water solubility, low bioavailability, and rapid systemic clearance. To overcome these limitations, we developed a liposomal delivery system for TQ and investigated its therapeutic potential in TNBC models via intravenous (IV) administration. In vitro results demonstrated enhanced cytotoxicity and apoptosis in TNBC cells with liposomal TQ (Lipo-TQ) compared to free TQ[8]. In vivo, IV-administered Lipo-TQ led to significant tumor regression, improved biodistribution, and reduced toxicity in xenograft mouse models. These findings suggest that liposomal encapsulation enhances the pharmacological properties of TQ, presenting Lipo-TQ as a novel and effective treatment strategy for TNBC.

INTRODUCTION

The history of cancer is rich and complex, spanning thousands of years below is a time line highlighting significant milestones in cancer research, treatment developments and notable books that have contributed to understanding of cancer. Cancer is the ancient disease which is found in the research of Hippocrates use the term “**carcinoma**” to describe tumors, in years 460-370 BCE. In earlier years chemotherapy was described in 1940. After the introduction of chemotherapy many drugs are introduced in the treatment of cancer. Every year, millions of people are diagnosed with cancer, which is the second leading cause of death worldwide after myocardial infarction. Fortunately, the number of cancer survivors is increasing, mainly due to advances in early detection and new treatment strategies. It has been reported that more than 15.5 million Americans with a history of cancer are alive by January 2016[1]

Unfortunately, chemotherapeutic agents create many adverse side effects. So instead of chemotherapeutic agent most of the scientists prefer the natural and herbal drug in the treatment of cancer. This natural and herbal drug has very less adverse effect as compared to chemotherapy drug. Many scientists are researching on this herbal drug to extract the active ingredient for the treatment of cancer. This active ingredient shows anticancer activity. So in this article we use *nigella sativa* as a herbal drug to extract thymoquinone (TQ). This *nigella sativa* has many properties for the treatment of various diseases and disorders. Such as, Anti-inflammatory, Antimicrobial Activity, Immunomodulation, Anticancer properties. The *nigella sativa* contains alkaloids, saponins, thymoquinone, essential oil, thymohydroquinone, nigellone, p-Cymene, dithymoquinone, carvacrol. In this *nigella sativa* the key compound is Thymoquinone (TQ) which shows anticancer activity.

Thymoquinone (TQ) acts as an anticancer agent. The chemical name of TQ is (2-methyl-5-isopropyl-1,4-benzoquinone) .[2]

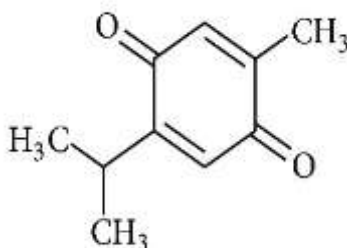


fig.no.1:- structure of thymoquinone

THE MECHANISMS OF ACTION TQ .

3.1 Apoptosis:-

TQ plays an important role in cancer management by activating tumor suppressor genes, phase II genes/enzymes, and peroxisome proliferator-activated receptors (PPARs), inhibiting the formation of new blood vessels and anti-inflammatory genes and inducing cell death.[3] There are various investigations that suggested TQ as a promising phytochemical that might be helpful for apoptosis to occur throughout different cancer cells due to its ability to cause apoptosis via the regulation of several pathways. TQ has been also shown to stimulate apoptosis in cells via a p53-dependent and p53-independent pathway and drug-induced apoptosis is attributed to caspase stimulation, up-regulation of p53 expression, down-regulation of anti-apoptotic genes [4]. Previous studies demonstrated that TQ exhibited anticancer properties and controlled apoptosis in doxorubicin-resistant human breast cancer cells (MCF-7/DOX cells) [5]. TQ causes apoptosis in DOX-resistant breast cancer cells by transcriptional overexpression of PTEN and amplified PTEN serves a remarkable part in preventing the phosphatidylinositol-3 kinase/Akt pathway and inducing p53 and p21 protein expression [6]. Furthermore, TQ modifies several pathways, including the inhibition of phase-I enzymes (cytochrome p450) and the stimulation of phase-II detoxification enzymes (glutathione transferase and N-acetyl transferase), the suppression of numerous signal transduction paths involved in promoting cell growth, cell invasion, and PPAR pathway stimulation. TQ suppresses NF-kappa-B activation, resulting in the downregulation of several inflammatory genes. A recent investigation reported that TQ interferes with TNF and NF-kappa-B signaling in the course of TQ-interfered apoptosis in cancer cells [7].

3.2 Cell Cycle Assay:-

❖ Mechanism of Action (MOA):-

3.2.1 Introduction to the Cell Cycle and Its Deregulation in Cancer:-

The cell cycle consists of four primary phases:

- G1 phase: Cell grows and prepares for DNA replication
- S phase: DNA replication occurs
- G2 phase: Cell prepares for mitosis
- M phase: Mitosis (cell division)

Progression through these phases is tightly regulated by cyclins, cyclin-dependent kinases (CDKs), and checkpoint proteins. In cancer, these checkpoints are often dysregulated, allowing uncontrolled proliferation. Thymoquinone (TQ) exerts anticancer activity by targeting these regulatory mechanisms, leading to cell cycle arrest, which halts tumor growth and promotes apoptosis.[8]

3.2.2 G0/G1 Phase Arrest By Thymoquinone:-

Key Molecular Targets of this mechanism are p53 (tumor suppressor), p21 and p27 (CDK inhibitors) Cyclin D1 / CDK4 / CDK6 complex

Mechanism:-

- TQ upregulates p53, which in turn increases p21 expression. p21 inhibits Cyclin D-CDK4/6 complex, preventing phosphorylation of Rb (Retinoblastoma protein).
- Hypophosphorylated Rb remains active and binds E2F, preventing transcription of S-phase genes.
- Then it is resulting Cell is arrested in G1 phase, and DNA replication is blocked.
- And Final Outcome comes Cancer cells are unable to enter S phase. Reduced proliferation and increased sensitivity to apoptosis.[9]

3.2.3 S Phase Suppression:-

- In some cancers, TQ has been shown to reduce the percentage of cells in the S phase, indicating a block in DNA synthesis.

Mechanism:- TQ downregulates cyclin A and CDK2, key regulators of S phase progression. May also interfere with DNA polymerases or induce DNA strand breaks via ROS.

- Then final resulting is Incomplete or stalled DNA replication. Activation of DNA damage response pathways. Entry into G2/M checkpoint arrest or apoptosis.[10]

3.2.4 G2/M Phase Arrest by Thymoquinone:-

- Key Molecular Targets are Cyclin B1 / CDK1 (CDC2), Checkpoint kinases (Chk1/Chk2) and Cdc25C phosphatase

Mechanism:- TQ increases ROS, causing DNA damage. ATM/ATR kinases activate Chk1/Chk2, which inhibit Cdc25C. Without active Cdc25C, CDK1 remains phosphorylated (inactive).

- Cyclin B1-CDK1 complex is unable to initiate mitosis.
- Then Cells are accumulate in G2 phase but cannot enter mitosis. Leads to mitotic catastrophe or apoptosis if damage is not repaired.[12]

3.2.5 ROS-Mediated DNA Damage and Cell Cycle Checkpoints:-

- TQ is a known ROS inducer. Moderate ROS can activate checkpoint signaling.
- ROS → DNA damage → Activation of ATM/ATR → p53/Chk1/Chk2 activation.

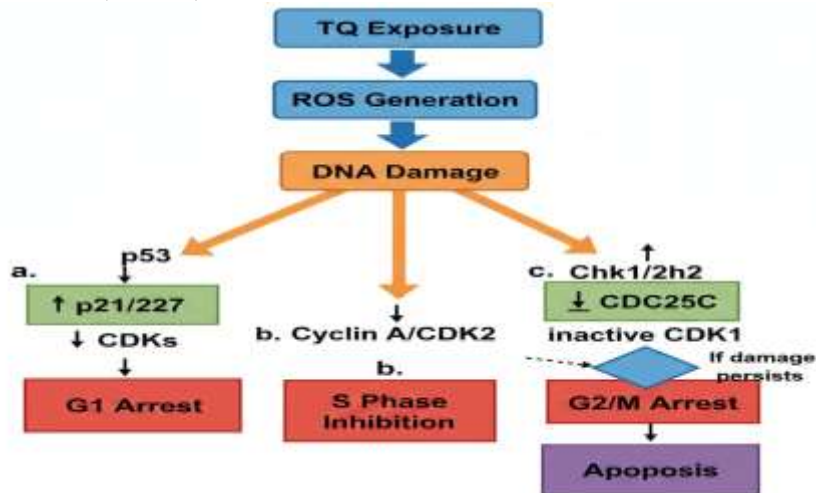
These pathways reinforce cell cycle arrest at G1/S or G2/M checkpoints. Prolonged arrest leads to apoptosis or senescence.[13]

3.2.6 Downstream Effects

Induction of Apoptosis by following arrest :-

- Pro-apoptotic proteins (e.g., Bax, caspase-3) are upregulated.
- Anti-apoptotic proteins (e.g., Bcl-2, survivin) are downregulated.
- Mitochondrial membrane potential collapses, leading to intrinsic apoptosis.[14]

3.2.7 Summary Flowchart (Textual):-



3.2.8 Implications for Cancer:-

- Therapy Blocks proliferation of tumor cells
- Sensitizes cells to chemo/radiation
- Minimal toxicity to normal cells due to their intact checkpoints [15].

3.3 PPAR-g PATHWAY:-

Mechanism of Action (MOA):-PPAR-γ Pathway Mediated by Thymoquinone in Anticancer Activities

3.3.1 Introduction:-

Thymoquinone (TQ), the main bioactive compound of *Nigella sativa* (black seed), has shown significant anticancer activity across multiple cancer types. One of the most critical molecular pathways involved in this action is the Peroxisome Proliferator-Activated Receptor gamma (PPAR-γ) pathway. PPAR-γ is a nuclear receptor that, when activated, can regulate key processes in cancer biology such as apoptosis, cell proliferation, inflammation, angiogenesis, and metastasis. TQ exerts its anticancer effect by activating this pathway and modulating the expression of PPAR-γ target genes.[16]

3.3.2 Activation of PPAR-γ by Thymoquinone:-

TQ acts as a natural modulator or ligand of PPAR-γ. While not a classical ligand, TQ either binds directly or increases the expression and activity of PPAR-γ. Once activated, PPAR-γ forms a heterodimer with the Retinoid X Receptor (RXR). This complex translocates into the nucleus, where it binds to specific DNA sequences known as PPAR Response Elements (PPREs) located in the promoter region of target genes. This binding modulates gene expression, turning on pro-apoptotic and anti-inflammatory genes, while suppressing oncogenes and survival-related genes.[17]

3.3.3 Downstream Effects in Cancer Cells:-

A. Induction of Apoptosis (Programmed Cell Death):-

- Upregulation of pro-apoptotic genes: Bax, p53, caspase-3, caspase-9. Downregulation of anti-apoptotic genes: Bcl-2, survivin.
- These changes lead to:- Mitochondrial membrane potential loss. Release of cytochrome c. Activation of the intrinsic caspase cascade leading to cell death.
- Selective killing of cancer cells without damaging normal cells.[18]

B. Inhibition of Cell Proliferation and Cell Cycle Arrest:-

- TQ-PPAR-γ activation suppresses cyclin D1 and CDK4/6, essential for G1/S phase transition. Simultaneously, it upregulates p21^{WAF1/Cip1} and p27^{Kip1}, which are cyclin-dependent kinase inhibitors.
- G1 phase arrest, halting the replication of cancer cells.[19]

C. Anti-Inflammatory Effects:-

- PPAR-γ activation by TQ inhibits NF-κB, a transcription factor that promotes inflammation and cancer progression. Downstream, this leads to: Decreased expression of COX-2, iNOS, and pro-inflammatory cytokines like IL-6, TNF-α. This anti-inflammatory action reduces chronic inflammation, a major contributor to cancer progression.[20]

D. Anti-Angiogenesis and Anti-Metastasis:-

- Angiogenesis inhibition: TQ downregulates VEGF (Vascular Endothelial Growth Factor), limiting blood vessel formation in tumors. Metastasis inhibition: TQ suppresses matrix metalloproteinases (MMP-2 and MMP-9), which degrade the extracellular matrix and facilitate invasion.
- TQ-PPAR- γ activation results in reduced invasion, migration, and metastasis of cancer cells.[21]

3.3.4 Experimental Support:-

- Several studies have confirmed the link between TQ, PPAR- γ , and anticancer effects[22].

3.3.5 Comprehensive Mechanism Flow:-

- Thymoquinone administration \rightarrow PPAR- γ expression/activation \uparrow \rightarrow PPAR- γ /RXR complex formation \rightarrow Nuclear translocation \rightarrow Binding to PPREs \rightarrow Transcriptional regulation of target genes [23].

3.3.6 Therapeutic Implications:-

- Selective Targeting: TQ selectively affects cancer cells while sparing normal cells. Adjuvant Therapy Potential: Can be combined with chemotherapeutic agents or PPAR- γ agonists (e.g., rosiglitazone) to enhance anticancer efficacy. Safety and Natural Origin: Being a plant-derived compound, TQ has shown low toxicity in preclinical models [24].

EFFECTIVE ROLE OF TQ IN TRIPLE NEGATIVE BREAST CANCER

DEFINITION:-

Triple Negative Breast Cancer (TNBC) is a type of breast cancer that is characterized by the absence of three common receptors known to fuel most breast cancer growth:

1. Estrogen receptors (ER)
2. Progesterone receptors (PR)
3. HER2 protein

Because TNBC lacks these receptors, it doesn't respond to hormonal therapies (like tamoxifen) or HER2-targeted treatments (like trastuzumab/Herceptin). This makes it more challenging to treat compared to other breast cancers [25].

According to this our TQ drug is acts on this type of cancer by several mechanisms:-

4.1 Antiproliferative Effects:-

Mechanism:-TQ inhibits the proliferation of TNBC cells such as MDA-MB-231, a commonly studied aggressive cell line. It induces cell cycle arrest, particularly at the G1/S or G2/M checkpoint, preventing cancer cells from multiplying.[26]

Pathways Affected:-

- PI3K/Akt/mTOR: This pathway promotes cell survival and growth in many cancers. TQ inhibits Akt phosphorylation, reducing proliferation.
- MAPK/ERK: TQ interferes with this signaling cascade, leading to reduced cellular replication.
- STAT3: TQ suppresses STAT3 activation, which is often hyperactive in TNBC and linked to tumor growth and immune evasion.[27]

4.2 Pro-apoptotic Activity:-

Mechanism:-TQ induces apoptosis by activating both intrinsic (mitochondrial) and extrinsic apoptotic pathways. It increases pro-apoptotic proteins like Bax, p53, and cytochrome c, while reducing anti-apoptotic proteins like Bcl-2 and survivin. Caspase activation (especially caspase-3 and caspase-9) is observed, which leads to programmed cell death.[28]

4.3 Anti-metastatic and Anti-angiogenic Properties:-

Mechanism:-

- TQ suppresses metastasis by downregulating MMP-2 and MMP-9, which are enzymes that degrade the extracellular matrix and allow cancer cells to invade. It also reduces expression of ICAM-1 and VCAM-1, molecules involved in cell adhesion and tumor migration.
- Anti-angiogenesis:-TQ reduces vascular endothelial growth factor (VEGF) and other pro-angiogenic signals, limiting the tumor's ability to form new blood vessels—an essential process for growth and metastasis.[29]

4.4 Modulation of Epigenetic and Immune Responses:-

- Epigenetic Modulation:-TQ affects epigenetic enzymes, including histone deacetylases (HDACs), leading to reactivation of tumor suppressor genes. It may also modulate microRNAs (miRNAs) that are dysregulated in TNBC.
- Immunomodulation:-TQ has shown potential to modulate immune cell activity, including:-Enhancing cytotoxic T-cell activity. Reducing immunosuppressive factors within the tumor microenvironment. These features could make TQ a potential adjuvant to immunotherapy, particularly PD-L1 inhibitors.[30]

4.5 Synergy with Chemotherapy and Resistance Reduction:-

- TQ shows synergistic effects with chemotherapeutic agents like doxorubicin, cisplatin, and paclitaxel.
- It sensitizes resistant TNBC cells to these drugs by:-Modulating efflux pumps (like P-glycoprotein). Reducing NF- κ B activity, a pathway linked to drug resistance. Inhibiting survivin and other resistance-related proteins.[31]

4.6 Drug Delivery and Bioavailability Challenges:-

- A key limitation is TQ's poor water solubility and bioavailability. Nanotechnology approaches such as TQ-loaded nanoparticles, liposomes, and polymeric micelles are being developed to improve delivery to tumors, particularly TNBC.[32]

ROUTES OF ADMINISTRATION OF THYMOQUINONE IN ANTICANCER ACTIVITY

By the bases of clinical research and clinical trials of thymoquinone we concluded that the oral route of administration has greater bioavailability of thymoquinone as compare to intravenous route. Intravenous route administration of TQ-NLC exhibited greater relative bioavailability compared to oral administration. It is postulated that the movement of TQ-NLC through the intestinal lymphatic system bypasses the first metabolism and therefore enhances the relative bioavailability. However, oral administration has a slower absorption rate compared to intravenous administration where the $AUC_{0-\infty}$ was 4.539 times lower than the latter.[33]

5.1 Oral Route of Thymoquinone Administration:-**Advantages:-**

- Patient-friendly: Non-invasive, easy to use, and suitable for chronic therapy.
- Cost-effective: Production and distribution of oral formulations are relatively cheap.
- Systemic effect: Useful for treating systemic conditions (e.g., inflammation, cancer, metabolic disorders).
- Suitable for long-term therapy: Ideal for daily dosing and preventive use.[34]

Disadvantages:-

- Low Bioavailability:-TQ is lipophilic with poor water solubility, limiting its dissolution and absorption in the GI tract. Undergoes first-pass metabolism in the liver, reducing the active drug in circulation.
- Chemical Instability:-TQ is sensitive to light, pH, and enzymatic degradation during digestion, affecting its therapeutic efficacy. Variable Absorption:-Food interactions and individual differences in gut flora, pH, or enzyme activity can affect absorption and efficacy.
- Strategies to Improve Oral Bioavailability:-Nanoformulations: Lipid-based carriers (e.g., nanoemulsions, liposomes) enhance solubility and absorption. Solid lipid nanoparticles (SLNs): Protect TQ and promote sustained release. Cyclodextrin complexes: Improve water solubility and chemical stability. Enteric-coated tablets or capsules: Protect TQ from acidic degradation in the stomach.[35]

5.2 Intravenous (IV) Route of Thymoquinone Administration:-**Advantages:-**

- 100% Bioavailability:IV injection bypasses the digestive system and first-pass metabolism, ensuring the entire dose enters systemic circulation. Rapid Onset of Action:-Useful in acute conditions, emergencies, or when immediate therapeutic effect is required (e.g., cancer or sepsis models).
- Controlled Dosing:-Allows precise control of plasma drug levels.[36]

Disadvantages:-

- Invasive Procedure:-Requires trained personnel and sterile conditions, which limits self-administration and increases healthcare costs.
- Formulation Challenges:-TQ is poorly soluble in water, making it difficult to prepare stable and safe IV formulations without suitable solubilizers or carriers.
- Risk of Adverse Effects:-Potential for injection site reactions, systemic toxicity, and allergic responses if formulation is not optimized.
- Approaches to Enable IV Use:-Solubilizing Agents: Use of surfactants or cosolvents to increase solubility. Encapsulation in carriers: Liposomes, micelles, or polymeric nanoparticles improve delivery and reduce toxicity. PEGylation or albumin-binding formulations: Enhance circulation time and reduce clearance.[37]

table. no. 1 :- oral vs intravenous thymoquinone

Feature	Oral Route	Intravenous Route
Bioavailability	Low due to poor solubility, First pass	100% (by passes absorption barrier)
Onset of action	Delayed (minutes to hours)	Immediate
Patient complains	Higher(non invasive)	Lower (requires medical administration)
Formulation challenge	Solubility and stability	Solubility ,safety of IV excipients
Cost	Lower	High
Use case	Long term therapy, Chronic condition	Acute treatment , Controlled dosing

According to this research we understand that the oral route have less bioavailability of TQ NLC ,So the motive of this article is TQ liposomal Preparation administrated through Intravenous route to make the more bioavailability, more therapeutic response and effective targeted delivery of TQ in anticancer activity.[38]

LIPOSOMAL THYMOQUINONE PREPARATION BY NANOFORMULATION THROUGH INTRAVENOUS (IV) ROUTE**6.1 Introduction :-**

- Triple Negative Breast Cancer (TNBC) is one of the most aggressive and hard-to-treat forms of breast cancer, characterized by the absence of estrogen, progesterone, and HER2 receptors. This makes conventional targeted therapies ineffective. Novel therapeutic agents such as thymoquinone (TQ), a phytochemical from *Nigella sativa*, have shown significant anticancer properties. However, the poor water solubility and rapid systemic clearance of TQ limit its clinical application.[39]

To overcome these challenges, liposomal nanoformulation of TQ presents a promising strategy, especially for intravenous (IV) administration, which allows systemic delivery with improved pharmacokinetics, tumor targeting, and reduced toxicity.[40]

6.2 Thymoquinone: Potential and Limitations :-

Thymoquinone (TQ) is a lipophilic monoterpene with broad pharmacological activities:

- Induces apoptosis in cancer cells via mitochondrial pathways
- Inhibits angiogenesis and metastasis
- Suppresses inflammation and oxidative stress

However, TQ suffers from:

- Low aqueous solubility
- Short biological half-life
- Limited oral bioavailability
- Non-specific biodistribution

Thus, developing a nanocarrier system like liposomes for TQ delivery becomes essential.[41]

6.3 Liposomal Delivery System: Rationale:-

Liposomes are spherical vesicles composed of phospholipid bilayers capable of encapsulating both hydrophilic and lipophilic drugs. For TQ, the lipophilic core of the bilayer is ideal for encapsulation, and liposomes offer:

- Improved drug solubility
- Reduced systemic toxicity
- Enhanced accumulation at tumor sites via the EPR effect
- Sustained drug release
- Biocompatibility and low immunogenicity

When administered intravenously, liposomal TQ bypasses gastrointestinal degradation and ensures direct systemic circulation.[42]

6.4 Materials and Composition:-

Table. No.2:- Materials and Composition

Component	Purpose
Phosphatidylcholine (PC)	Forms lipid bilayer
Cholesterol	Enhance stability and fluidity
DSPE-PEG 2000 (optional)	Provides stealth properties (long circulation)
Thymoquinone (TQ)	Active anti cancer agent
Chloroform, methanol	Organic solvents from lipid dissolution
PSB or ammonium sulphate	Hydration medium

6.5 Preparation Method: Thin Film Hydration + Sonication:-

Step-by-Step Protocol:

1. Lipid Phase Formation

Dissolve phospholipids, cholesterol, and thymoquinone in a 2:1 (v/v) chloroform:methanol mixture.

2. Film Formation

Evaporate the solvent using a rotary evaporator at 45°C under vacuum until a thin, dry lipid film forms on the flask wall.

3. Hydration:-Hydrate the lipid film with warm phosphate-buffered saline (PBS) or ammonium sulfate solution at 60°C, forming multilamellar vesicles (MLVs).

4. Size Reduction

Sonicate the dispersion using a probe sonicator or extrude through membranes (200–100 nm) to achieve nano-sized vesicles.

5. Purification

Remove free TQ and excess components by dialysis or centrifugation.

6. Sterilization for IV Use

Sterilize via 0.22 µm filtration before injection into animal models or patients.[43]

6.6 Characterization of Nanoformulation:-

Table.no.3:- Characterization of Nanoformulation

Parameter	Methods	Purpose
Particle size and PDI	Dynamic light scattering (DLS)	Ensures nanoscale range and homogeneity
Zeta potential	Zetasizer	Measures surface charge and predicts stability
Morphology	TEM/SEM	Visual confirmation of structure
Encapsulation efficiency	UV-Vis or HPLC analysis	Calculates % of drug loaded inside liposomes
Drug release profile	In vitro dialysis	Studies release kinetics over time
Stability	Storage at 4 C at room temprature	Monitors aggregation and leakage

6.7 Intravenous Administration and In Vivo Studies:-

Animal Models:-

- Mice or rats bearing TNBC xenografts (e.g., MDA-MB-231 cells)

Administration Route:

- IV injection via tail vein
- Evaluated Parameters:
- Tumor size reduction
- Survival analysis
- Organ toxicity (via histopathology)
- Biodistribution (fluorescent or radioactive tagging)
- Expression of apoptotic markers (e.g., Bax, Bcl-2, caspase-3)[44]

6.8 Mechanisms of Anticancer Action in TNBC:-

- Apoptosis induction: Through caspase activation, ROS generation, mitochondrial dysfunction
- Cell cycle arrest: At G2/M or S phase
- Inhibition of metastasis: Downregulation of MMPs and EMT markers
- Anti-angiogenesis: Decrease in VEGF expression
- Anti-inflammatory effects: Suppression of NF-κB pathway
- Liposomal delivery enhances these actions by increasing TQ’s cellular uptake and retention within the tumor microenvironment.[45]

6.9 Advantages Over Free TQ:-

Table.no:- Advantages Over Free TQ

Free TQ	Liposomal TQ (nanoformulation)
Poor solubility	High solubility in lipid bilayer
Rapid clearance	Prolonged Circulation time
Non specific distribution	Preferential Tumor accumulation (EPR effect)
Dose limiting toxicity	Reduced systemic side effect
Short therapeutic window	Sustained release for Prolonged efficacy

6.10 Future Directions:-

Surface targeting: Conjugating ligands (e.g., folate, transferrin, antibodies) to actively target TNBC cells

- Combination therapy: Co-encapsulation of TQ with chemotherapeutics or siRNA
- Theranostics: Incorporating imaging agents for real-time monitoring
- Clinical translation: Scale-up production, GLP/GMP compliance, clinical trials [46].

CONCLUSION :-

This study provides compelling evidence that intravenous administration of liposomal thymoquinone represents a promising new therapeutic approach for treating triple-negative breast cancer. By overcoming the physicochemical limitations of free TQ, the liposomal formulation ensures enhanced delivery, greater tumor selectivity, and reduced systemic toxicity. Lipo-TQ not only significantly suppressed TNBC tumor growth in vitro and in vivo but also displayed a favorable safety profile. Given these findings, Lipo-TQ has strong potential as an adjunct or standalone therapy for TNBC and warrants further investigation through clinical trials. Future research should focus on combination strategies with existing chemotherapies, evaluation of resistance pathways, and personalized delivery systems to maximize therapeutic outcomes[45,46,47]

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