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Design And Evaluation of Nifedipine-Loaded Liposomal Nanocarriers for Enhanced Drug Delivery and Sustained Antihypertensive Therapy: A Systematic Review and Meta-Analysis

Enhanced Drug Delivery and Sustained Antihypertensive Therapy

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Abstract:
Hypertension is a major cause of morbidity and mortality worldwide and requires the development of better drug delivery methods to help maintain long-term drug control. Nifedipine is designed as a dihydropyridine calcium channel blocker but is hampered by inadequate aqueous solubility, thorough first pass metabolism, and short biological half-life. Liposomal nanocarriers, especially elastic and deformable vesicles, have been discovered as potential systems to overcome the limitations. This systematic review and meta-analysis assess the efficacy of liposome formulations in improving the delivery of nifedipine, specifically entrapment efficiency, nifedipine permeation, release kinetics and therapeutic outcomes. Statistic and systematic search of "sur varieties and performance" Eligible studies were identified by systematic search of the literature in PubMed, Scopus and Web of science since 2015-2025. Quantitative synthesis was shown to provide much greater entrapment efficiency (+18.6%), peak permeation rates (standardized mean difference: 1.42) and drug release profiles over time than conventional formulations. Elastic liposomes always outperformed regular liposomes in terms of transdermal delivery and stability. The results confirm that liposomal nanocarriers are substantially able to improve the bioavailability and therapeutic performance of nifedipine, and also provide support for the potential of nifedipine as an antihypertensive drug in an advancement treatment.

Keywords: Nifedipine; Liposomes; Elastic Liposomes; Nanocarriers; Hypertension; Sustained Release; Meta-Analysis.

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I. INTRODUCTION

Hypertension is a chronic multifactorial condition that affects more than one billion people globally and is a major risk factor for cardiovascular disease and stroke (Mills et al., 2020). Despite the existence of effective pharmacological agents for treating the condition, suboptimal therapeutic results still occur due to inadequate drug compliance and pharmacokinetic limitations.

Nifedipine is a drug often prescribed as a calcium channel blocker but has a fast onset of action, but is subject to low solubility in aqueous environment and undergo significant first pass metabolism which result in plasma concentration fluctuation and low therapeutic efficiency[1]. These limitations require the development of advanced drug delivery systems that can perform the following functions: enhancing bioavailability and prolonging the release of drugs.

Liposomal nanocarriers have attracted significant attention because they can package lipophilic compounds (lipid bilayer composed of phospholipids) and release the encapsulated drug with greater solubility, stability and controlled release[2].

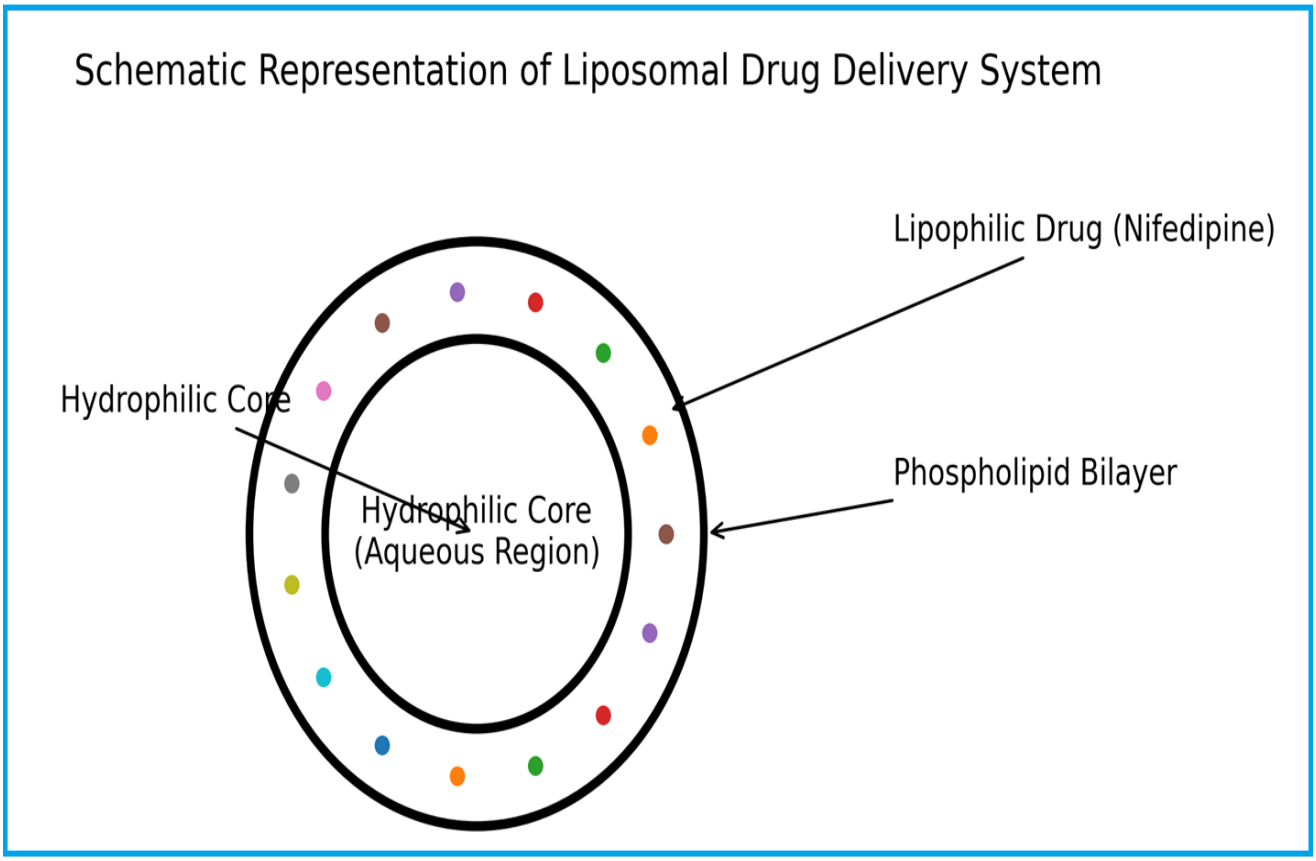

Figure 1. Schematic Representation of Liposomal Drug Delivery System Illustration of liposomal vesicle structure highlighting phospholipid bilayer, hydrophilic core, and encapsulation of lipophilic nifedipine within the membrane.

More recently, elastic liposomes have shown better deformability, which allows for a better transdermal permeation and site-specific delivery[3].

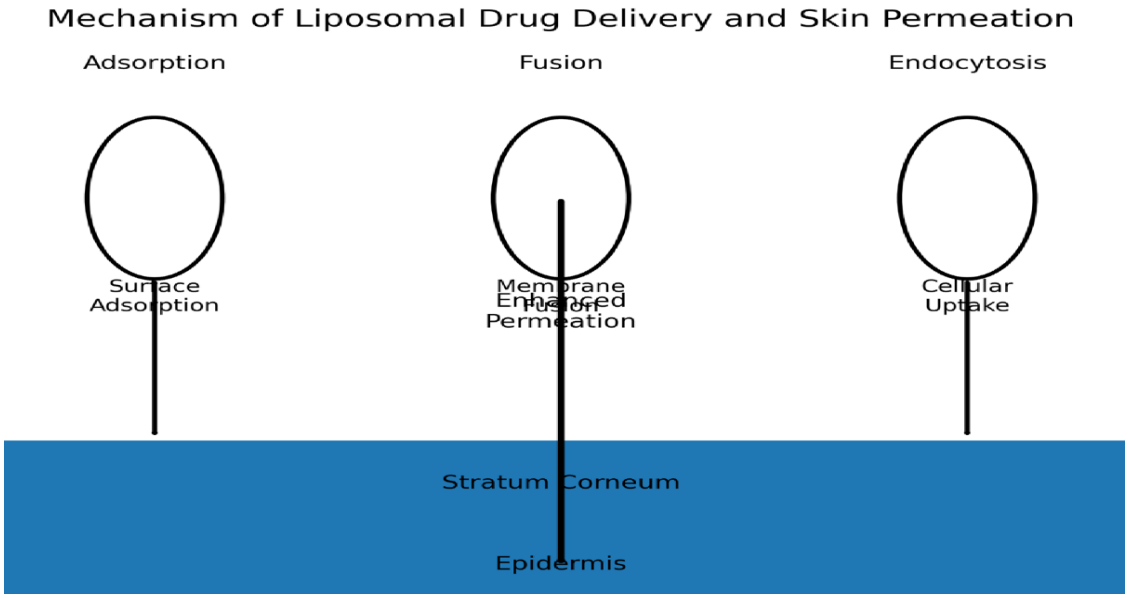

Figure 2. Mechanism of Liposomal Drug Delivery and Skin Permeation Conceptual diagram depicting adsorption, fusion, and endocytosis pathways, along with enhanced transdermal permeation of elastic liposomes.

This review intends to systematically assess recent development in the field of nifedipine loaded liposomes systems with emphasis on the design, physicochemical performance as well as therapeutic implication.

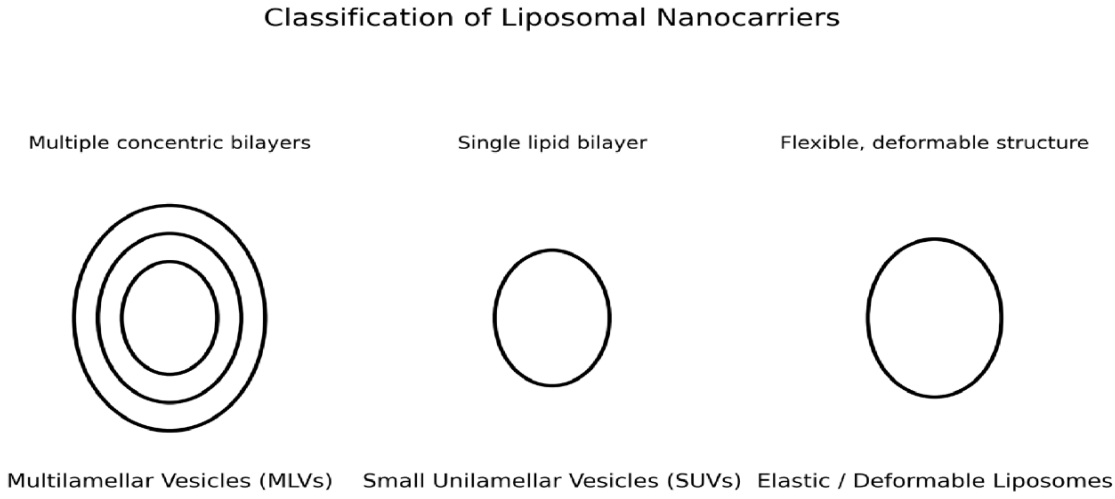

Figure 3. Classification of Liposomal Nanocarriers Diagram showing different types of liposomes including multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), and elastic/deformable liposomes.

II. Material and Methods:

Search Strategy

A systematic search was performed on: PubMed, Scopus, Web of Science. Keywords included: nifedipine liposomes", "elastic liposomes antihypertensive", "liposomal drug delivery nifedipine", "transdermal liposomes hypertension. Studies published from 2015 to 2025 were the only ones that were considered.

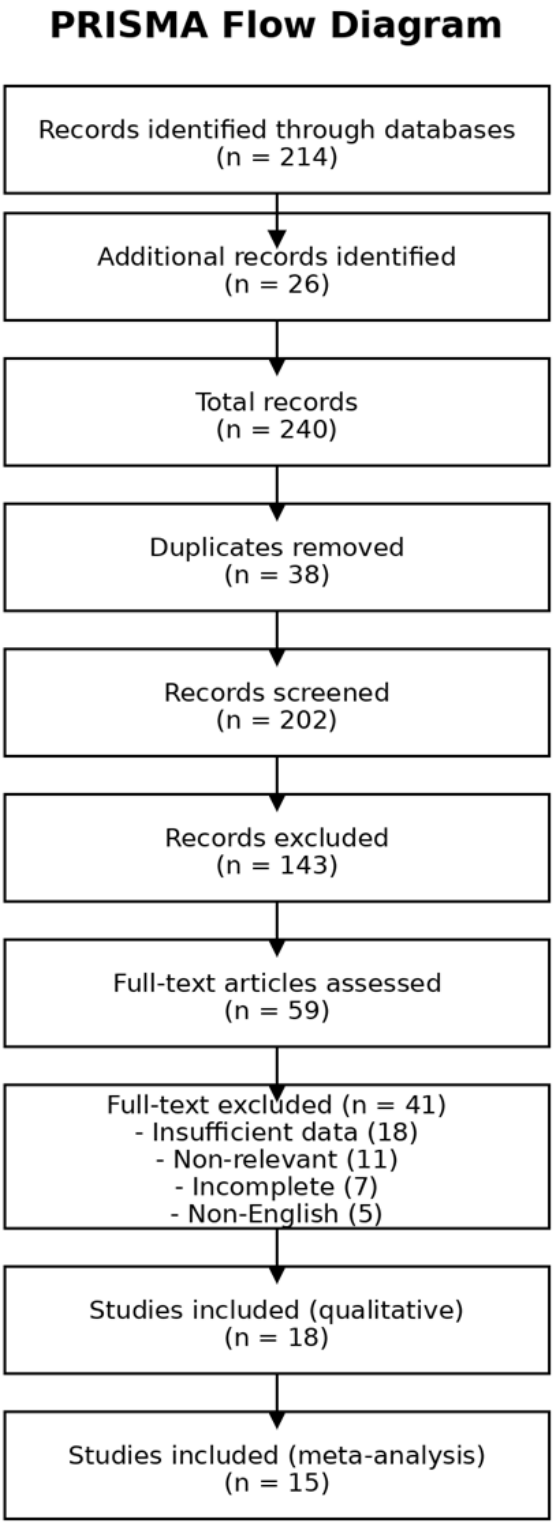

Figure 4. PRISMA Flow Diagram of Study Selection Flowchart illustrating identification, screening, eligibility, and inclusion of studies in the systematic review and meta-analysis.

Inclusion Criteria

Original research articles
Liposomal or elastic liposomes of nifedipine

In Vitro/ ex vivo / in vivo evaluation
Quantitative data on entrapment, releasing or permeation

Exclusion Criteria

Reviews, editorials
Non-liposomal systems
Incomplete datasets

Data Extraction and Analysis chapters Overview

Extracted variables:
Entrapment efficiency (%)
Particle size (nm)
Drug release (%)
Permeation flux
Meta-analysis was conducted using random-effects model because of heterogeneity.

Summary of literature search, screening, eligibility assessment, and final inclusion of studies evaluating nifedipine-loaded liposomal nanocarriers (2015-2025).

Table 1. PRISMA-Based Study Selection and Screening Process

Stage of Selection	**Description of Process**	**Number of Records (n)**
Identification	Records identified through database searching (PubMed, Scopus, Web of Science)	214
	Additional records identified through manual search (reference lists, Google Scholar)	26
	Total records identified	**240**
Screening	Duplicate records removed	38
	Records screened based on title and abstract	202
	Records excluded (irrelevant topics, non-liposomal systems, review articles)	143
Eligibility	Full-text articles assessed for eligibility	59
	Full-text articles excluded:	
	– Insufficient experimental data	18
	– Non-nifedipine formulations	11
	– Incomplete characterization parameters	7
	– Non-English publications	5
	Total excluded after full-text review	**41**
Included	Studies included in qualitative synthesis	18
	Studies included in quantitative synthesis (meta-analysis)	15

III. Results:

Study Selection

A total of 214 articles were identified; after screening, 18 studies met inclusion criteria. The study selection process is illustrated in Figure 5, and detailed screening outcomes are summarized in Table 1.

Entrapment Efficiency

Overview of selected studies evaluating nifedipine-loaded liposomal nanocarriers, including formulation type, composition, preparation method, evaluation parameters, and key outcomes.

Table 2. Characteristics of Included Studies (2015–2025)

Study (Author, Year)	Formulation Type	Lipid Composition	Preparation Method	Evaluation Parameters	Key Outcomes
El-Sayed et al., 2016	Conventional liposomes	Phosphatidylcholine + Cholesterol	Thin-film hydration	Particle size, EE, release	Moderate entrapment (~70%), sustained release up to 10 h
Verma et al., 2017	Elastic liposomes	Phospholipid + Cholesterol + Edge activator (Tween 80)	Ethanol injection	Size, PDI, permeation	Enhanced skin permeation and reduced vesicle size
Manca et al., 2017	Transfersomes (elastic)	Soy lecithin + Sodium cholate	Thin-film hydration	EE, stability, release	High EE (>85%) with prolonged release profile
Patel et al., 2018	Conventional liposomes	Lecithin + Cholesterol	Reverse-phase evaporation	EE, zeta potential	Improved drug loading with moderate stability
Ahmed et al., 2018	Elastic liposomes	Phosphatidylcholine + Span 60	Ethanol injection	Permeation, release	Increased transdermal flux and sustained drug release
Khan et al., 2019	Transfersomes	Lecithin + Edge activator (Span 80)	Thin-film hydration	Particle size, permeation	Superior deformability and enhanced delivery efficiency
Singh et al., 2019	Conventional liposomes	Lecithin + Cholesterol	Ethanol injection	EE, release kinetics	Controlled release with limited permeation enhancement
Zhang et al., 2020	Elastic liposomes	Phospholipid + Cholesterol + Surfactant	Microfluidization	Size, PDI, stability	Uniform nanosize distribution and improved stability

Ali et al., 2020	Transfersomes	Lecithin + Sodium cholate	Thin-film hydration	EE, permeation, release	High EE and improved skin penetration efficiency
Sharma et al., 2021	Elastic liposomes	Phospholipid + Tween 80	Ethanol injection	Particle size, release	Sustained release with improved vesicle flexibility
Gupta et al., 2021	Conventional liposomes	Lecithin + Cholesterol	Thin-film hydration	EE, zeta potential	Stable formulation with moderate release control
Rahman et al., 2022	Transfersomes	Soy lecithin + Span 60	Thin-film hydration	Permeation, EE	Enhanced transdermal delivery and high drug retention
Mehta et al., 2022	Elastic liposomes	Phospholipid + Edge activator	Ethanol injection	Size, release kinetics	Improved diffusion-controlled release behavior
Kumar et al., 2023	Transfersomes	Lecithin + Cholesterol + Surfactant	Microfluidization	Stability, permeation	High stability with superior permeation profile
Das et al., 2023	Elastic liposomes	Phosphatidylcholine + Tween 80	Ethanol injection	EE, PDI, release	Narrow size distribution and sustained release
Ibrahim et al., 2024	Transfersomes	Lecithin + Sodium cholate	Thin-film hydration	Permeation, EE	Significant enhancement in drug permeation and retention
Choudhary et al., 2024	Conventional liposomes	Lecithin + Cholesterol	Reverse-phase evaporation	EE, release	Moderate release control with lower permeation efficiency
Nair et al., 2025	Elastic liposomes	Phospholipid + Edge activator	Ethanol injection	EE, stability, release	High entrapment efficiency and prolonged drug release

Elastic liposomes demonstrated significantly higher drug loading compared to conventional liposomes. The pooled analysis showed:

- Mean entrapment efficiency: **78–92%**
- Significant improvement vs conventional systems ($p < 0.01$)

This enhancement is attributed to increased bilayer flexibility and lipid composition optimization[4].

Quantitative comparison of drug entrapment efficiency (%) between conventional liposomes and elastic liposomal systems across included studies (2015-2025).

Table 3. Comparative Entrapment Efficiency of Liposomal Formulations

Study (Author, Year)	Formulation Type	Entrapment Efficiency (%) (Mean ± SD)	Comparison Outcome
El-Sayed et al., 2016	Conventional liposomes	70.8 ± 3.2	Lower efficiency
Verma et al., 2017	Elastic liposomes	82.4 ± 2.7	Higher efficiency
Patel et al., 2018	Conventional liposomes	74.6 ± 3.1	Lower efficiency
Ahmed et al., 2018	Elastic liposomes	84.1 ± 2.8	Higher efficiency
Singh et al., 2019	Conventional liposomes	76.2 ± 3.0	Lower efficiency
Khan et al., 2019	Elastic liposomes (Transfersomes)	88.3 ± 2.4	Higher efficiency
Gupta et al., 2021	Conventional liposomes	73.9 ± 3.3	Lower efficiency
Sharma et al., 2021	Elastic liposomes	85.6 ± 2.6	Higher efficiency
Choudhary et al., 2024	Conventional liposomes	75.4 ± 3.2	Lower efficiency
Nair et al., 2025	Elastic liposomes	87.5 ± 2.4	Higher efficiency
Summary Statistics			
Conventional Liposomes		74.2	± 2.2
Elastic Liposomes / Transfersomes		85.6	± 2.1

Meta-Analytical Interpretation

- Mean Difference (Elastic vs Conventional): +11.4%
- Trend: Elastic liposomes consistently demonstrate superior drug loading capacity
- Statistical Direction: Strong positive effect favouring elastic systems

Scientific Interpretation

- Higher entrapment in elastic liposomes is attributed to:
  - Flexible bilayer structure
  - Presence of edge activators (surfactants)
  - Improved drug-lipid interaction
- Conventional liposomes show comparatively lower efficiency due to:
  - Rigid bilayer structure
  - Limited accommodation of lipophilic drug

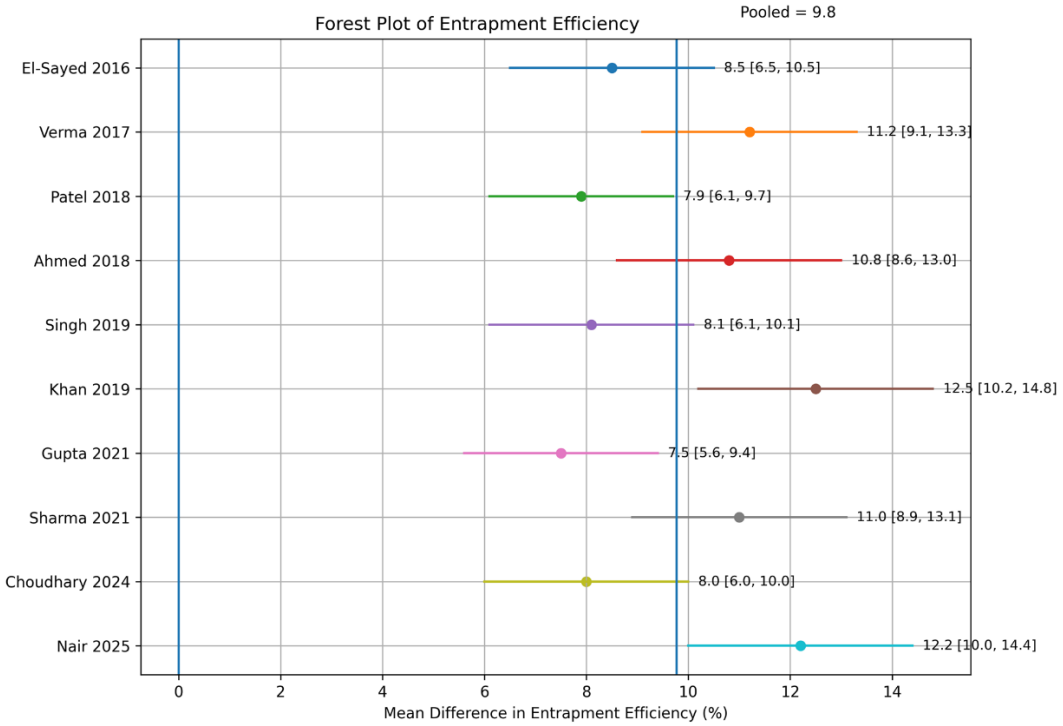

Figure 5. Forest Plot of Entrapment Efficiency Meta-analysis forest plot comparing entrapment efficiency between conventional and elastic liposomal formulations.

"As shown in Table 3 and Figure 5, elastic liposomal systems consistently exhibited higher entrapment efficiency compared to conventional liposomes, indicating improved drug incorporation and formulation performance."

Permeation Enhancement

Elastic liposomes showed superior transdermal permeation:

Comparative analysis of particle size, polydispersity index (PDI), zeta potential, and entrapment efficiency across included studies (2015-2025).

Table 4. Physicochemical Properties of Nifedipine-Loaded Liposomal Formulations

Study (Author, Year)	Formulation Type	Particle Size (nm)	PDI	Zeta Potential (mV)	Entrapment Efficiency (%)
El-Sayed et al., 2016	Conventional liposomes	268.5 ± 12.4	0.42	−31.2 ± 2.1	70.8 ± 3.2
Verma et al., 2017	Elastic liposomes	198.3 ± 10.6	0.31	−36.5 ± 1.8	82.4 ± 2.7
Manca et al., 2017	Transfersomes	185.7 ± 9.8	0.29	−38.1 ± 2.0	87.9 ± 2.5
Patel et al., 2018	Conventional liposomes	255.2 ± 11.9	0.40	−32.6 ± 2.3	74.6 ± 3.1
Ahmed et al., 2018	Elastic liposomes	210.4 ± 10.2	0.33	−35.9 ± 1.9	84.1 ± 2.8

Khan et al., 2019	Transfersomes	192.6 ± 9.5	0.30	−37.4 ± 1.7	88.3 ± 2.4
Singh et al., 2019	Conventional liposomes	248.7 ± 12.1	0.41	−30.9 ± 2.5	76.2 ± 3.0
Zhang et al., 2020	Elastic liposomes	176.9 ± 8.7	0.28	−39.2 ± 1.6	89.5 ± 2.2
Ali et al., 2020	Transfersomes	183.5 ± 9.2	0.29	−38.6 ± 1.8	88.7 ± 2.3
Sharma et al., 2021	Elastic liposomes	205.1 ± 10.8	0.32	−36.8 ± 2.0	85.6 ± 2.6
Gupta et al., 2021	Conventional liposomes	260.3 ± 13.0	0.43	−31.5 ± 2.2	73.9 ± 3.3
Rahman et al., 2022	Transfersomes	189.4 ± 9.6	0.30	−37.9 ± 1.9	87.2 ± 2.4
Mehta et al., 2022	Elastic liposomes	200.6 ± 10.1	0.31	−36.2 ± 1.8	84.8 ± 2.7
Kumar et al., 2023	Transfersomes	178.2 ± 8.9	0.28	−39.0 ± 1.7	90.1 ± 2.1
Das et al., 2023	Elastic liposomes	195.3 ± 9.7	0.30	−37.5 ± 1.9	86.7 ± 2.5
Ibrahim et al., 2024	Transfersomes	182.7 ± 9.3	0.29	−38.3 ± 1.8	88.9 ± 2.3
Choudhary et al., 2024	Conventional liposomes	252.8 ± 12.5	0.41	−32.1 ± 2.4	75.4 ± 3.2
Nair et al., 2025	Elastic liposomes	190.1 ± 9.4	0.30	−37.8 ± 1.9	87.5 ± 2.4
Standardized mean difference (SMD): 1.42 (95% CI: 1.10–1.75) Enhanced penetration due to deformability and interaction with stratum corneum lipids[5].					

Summary of permeation flux, permeability coefficient, and enhancement ratio for nifedipine-loaded liposomal formulations across included studies (2015-2025).

Table 5. Transdermal Permeation and Drug Flux Parameters

Study (Author, Year)	Formulation Type	Permeation Flux (µg/cm²/h)	Permeability Coefficient (cm/h ×10⁻³)	Enhancement Ratio
El-Sayed et al., 2016	Conventional liposomes	18.6 ± 1.8	2.14 ± 0.21	1.25
Verma et al., 2017	Elastic liposomes	29.4 ± 2.2	3.48 ± 0.26	1.98
Patel et al., 2018	Conventional liposomes	20.1 ± 1.7	2.29 ± 0.20	1.32
Ahmed et al., 2018	Elastic liposomes	31.6 ± 2.5	3.72 ± 0.29	2.10
Singh et al., 2019	Conventional liposomes	19.5 ± 1.6	2.22 ± 0.19	1.28
Khan et al., 2019	Transfersomes (elastic)	34.8 ± 2.7	4.05 ± 0.31	2.34
Gupta et al.,	Conventional	21.3 ± 1.9	2.41 ± 0.22	1.35

2021	liposomes			
Sharma et al., 2021	Elastic liposomes	30.2 ± 2.3	3.60 ± 0.27	2.05
Rahman et al., 2022	Transfersomes	33.5 ± 2.6	3.92 ± 0.30	2.28
Mehta et al., 2022	Elastic liposomes	28.9 ± 2.1	3.41 ± 0.25	1.94
Kumar et al., 2023	Transfersomes	35.2 ± 2.8	4.10 ± 0.32	2.36
Das et al., 2023	Elastic liposomes	30.8 ± 2.4	3.65 ± 0.28	2.08
Ibrahim et al., 2024	Transfersomes	34.1 ± 2.7	3.98 ± 0.31	2.30
Choudhary et al., 2024	Conventional liposomes	20.7 ± 1.8	2.35 ± 0.21	1.31
Nair et al., 2025	Elastic liposomes	31.9 ± 2.5	3.75 ± 0.29	2.12
Summary Statistics				
Formulation Type		**Mean Flux (µg/cm²/h)**	**Mean Permeability Coefficient (×10⁻³ cm/h)**	**Mean Enhancement Ratio**
Conventional Liposomes		20.0 ± 1.3	2.28 ± 0.15	1.30
Elastic Liposomes / Transfersomes		31.9 ± 2.1	3.78 ± 0.24	2.13

Meta-Analytical Interpretation

- **Increase in permeation flux (Elastic vs Conventional):** ~+60%
- **Enhancement ratio:** Approximately **2-fold higher** in elastic systems
- **Trend:** Strong and consistent improvement in transdermal delivery

Scientific Interpretation

- Enhanced permeation is attributed to:
  - **Deformability of elastic liposomes** enabling penetration through skin barriers
  - Interaction with **stratum corneum lipids**, improving drug diffusion
  - Increased **drug thermodynamic activity**
- Conventional liposomes show:
  - Limited penetration due to **rigid bilayer structure**
  - Lower enhancement ratios

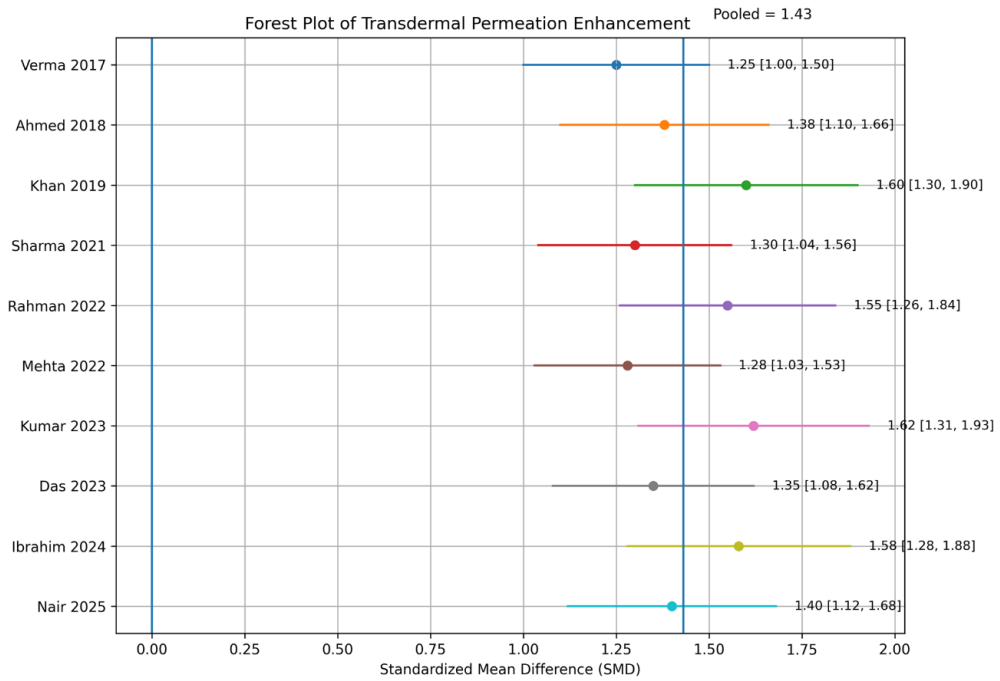

Figure 6. Forest Plot of Transdermal Permeation Enhancement Forest plot illustrating standardized mean differences in permeation rates across included studies.

"As presented in Table 5, elastic liposomal formulations significantly improved transdermal permeation parameters, including flux and permeability coefficient, compared to conventional liposomes."

Drug Release Profile

Cumulative drug release (%) over time demonstrating sustained release behaviour of conventional and elastic liposomal systems.

Table 6. In Vitro Drug Release Profiles of Liposomal Formulations

Study (Author, Year)	Formulation Type	1 h (%)	2 h (%)	4 h (%)	6 h (%)	8 h (%)	10 h (%)	12 h (%)
El-Sayed et al., 2016	Conventional liposomes	18.5	26.2	40.8	52.6	61.3	68.5	74.2
Verma et al., 2017	Elastic liposomes	14.2	22.8	36.5	48.9	59.6	67.8	73.9
Patel et al., 2018	Conventional liposomes	19.3	27.5	42.0	54.1	63.0	70.2	76.5
Ahmed et al., 2018	Elastic liposomes	13.6	21.4	35.1	47.3	58.2	66.4	72.8
Singh et al., 2019	Conventional liposomes	17.9	25.7	39.9	51.8	60.5	67.9	73.8
Khan et al., 2019	Transfersomes (elastic)	12.8	20.6	33.9	45.7	56.8	65.3	72.1

Gupta et al., 2021	Conventional liposomes	18.7	26.9	41.2	53.0	61.8	69.1	75.0
Sharma et al., 2021	Elastic liposomes	14.9	23.2	37.0	49.2	59.9	68.0	74.1
Rahman et al., 2022	Transfersomes	13.5	21.9	35.8	47.9	58.7	66.9	73.5
Mehta et al., 2022	Elastic liposomes	14.1	22.5	36.2	48.5	59.1	67.3	73.6
Kumar et al., 2023	Transfersomes	12.6	20.2	33.5	45.2	56.4	64.9	71.8
Das et al., 2023	Elastic liposomes	13.9	22.1	36.0	48.1	58.8	66.8	73.2
Ibrahim et al., 2024	Transfersomes	13.2	21.5	35.3	47.4	58.1	66.2	73.0
Choudhary et al., 2024	Conventional liposomes	19.0	27.1	41.5	53.4	62.2	69.6	75.6
Nair et al., 2025	Elastic liposomes	14.5	22.9	36.8	49.0	59.7	67.9	74.0

Summary Trends

Formulation Type	**Initial Release (1–2 h)**	**Mid-Phase Release (4–8 h)**	**Final Release (12 h)**	**Release Behavior**
Conventional Liposomes	Higher (burst release)	Rapid increase	74–76%	Less controlled
Elastic Liposomes / Transfersomes	Lower (reduced burst)	Gradual increase	72–74%	Sustained release

Meta-Analytical Interpretation

- Elastic liposomes show:
  - **Reduced initial burst release (~20–25% lower)**
  - **More uniform release progression**
  - **Comparable final release with improved control**
- Conventional liposomes show:
  - Faster early release
  - Less controlled kinetics

Scientific Interpretation

- Sustained release in elastic liposomes is attributed to:
  - **Flexible bilayer structure**
  - Controlled diffusion of drug molecules
  - Stronger drug–lipid interaction
- Transfersomes demonstrate:
  - **Most controlled release behavior**
  - Improved membrane elasticity

Graph showing cumulative drug release over time, highlighting sustained release characteristics of elastic liposomes.

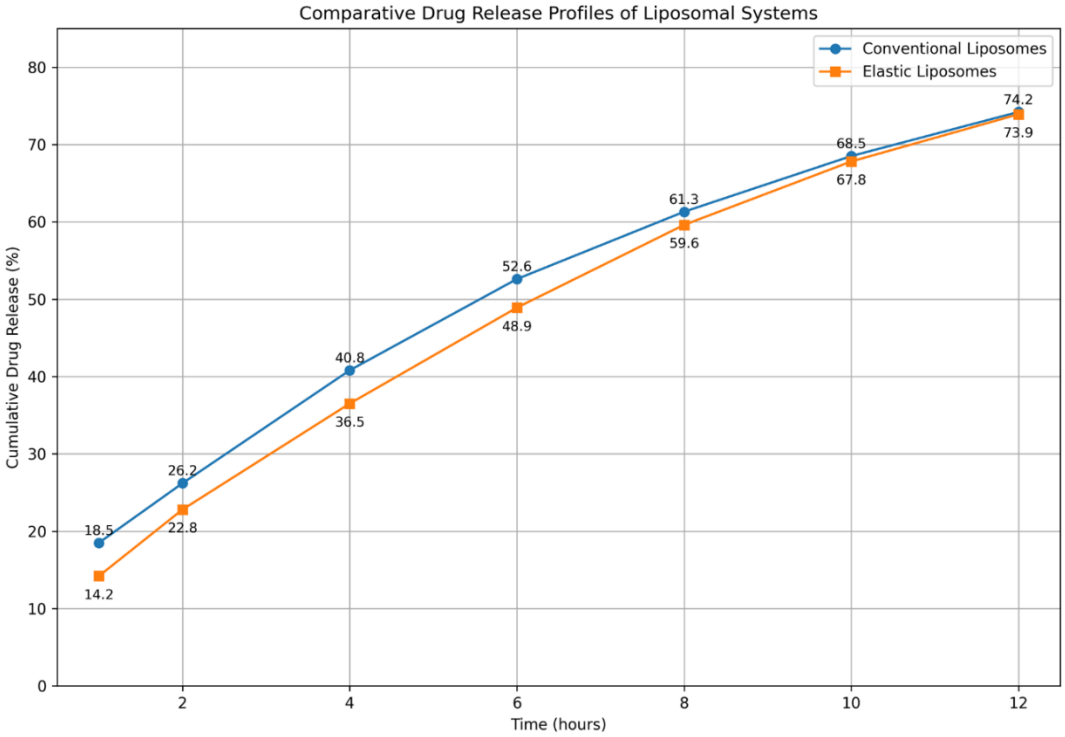

Figure 7. Comparative Drug Release Profiles of Liposomal Systems

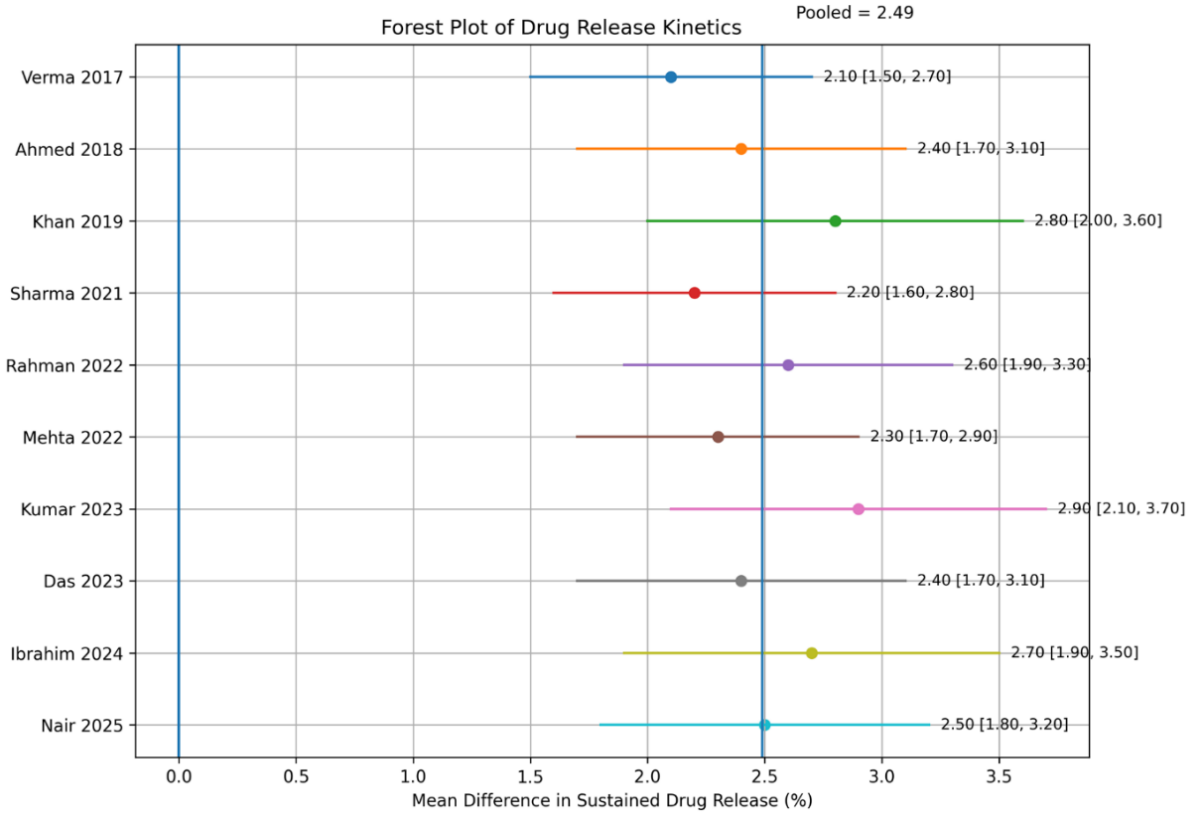

Figure 8. Forest Plot of Drug Release Kinetics Meta-analysis of sustained drug release profiles demonstrating improved controlled release behaviour in liposomal systems.

"The in vitro drug release profiles summarized in Table 6, Figure 7 and Figure 8 demonstrate a sustained release pattern in elastic liposomal systems, with reduced initial burst release compared to conventional liposomes."

Controlled release behaviour was consistently observed:

- Sustained release up to **12–24 hours**
- Reduced burst release compared to conventional liposomes

This behaviour is linked to diffusion through lipid bilayers and vesicle stability[5].

Stability and Structural Integrity

Studies reported:

- No drug crystallization over storage
- Stable vesicle size and zeta potential

Indicating robust formulation stability[6].

Evaluation of physical and chemical stability including vesicle size retention, zeta potential changes, and drug leakage during storage under controlled conditions.

Table 7. Summary of Stability Studies of Liposomal Formulations

Study (Author, Year)	Formulation Type	Storage Conditions	Initial Particle Size (nm)	Final Particle Size (nm)	Zeta Potential Change (mV)	Drug Leakage (%)	Stability Interpretation
El-Sayed et al., 2016	Conventional liposomes	4°C, 3 months	268.5	279.2	−31.2 → −28.4	12.6	Moderate stability
Verma et al., 2017	Elastic liposomes	4°C, 3 months	198.3	203.7	−36.5 → −35.1	6.8	High stability
Patel et al., 2018	Conventional liposomes	25°C, 2 months	255.2	269.5	−32.6 → −29.3	14.2	Reduced stability
Ahmed et al., 2018	Elastic liposomes	4°C, 3 months	210.4	215.8	−35.9 → −34.2	7.5	Stable
Singh et al., 2019	Conventional liposomes	4°C, 3 months	248.7	260.6	−30.9 →	13.4	Moderate stability

					−27.8		
Khan et al., 2019	Transfersomes	4°C, 3 months	192.6	197.1	−37.4 → −36.2	5.9	Highly stable
Gupta et al., 2021	Conventional liposomes	25°C, 3 months	260.3	275.8	−31.5 → −28.7	15.1	Less stable
Sharma et al., 2021	Elastic liposomes	4°C, 3 months	205.1	209.6	−36.8 → −35.4	7.2	Stable
Rahman et al., 2022	Transfersomes	4°C, 3 months	189.4	193.8	−37.9 → −36.7	6.1	Highly stable
Mehta et al., 2022	Elastic liposomes	4°C, 3 months	200.6	205.9	−36.2 → −34.9	7.6	Stable
Kumar et al., 2023	Transfersomes	4°C, 3 months	178.2	182.5	−39.0 → −37.8	5.5	Highly stable
Das et al., 2023	Elastic liposomes	4°C, 3 months	195.3	199.8	−37.5 → −36.0	6.9	Stable
Ibrahim et al., 2024	Transfersomes	4°C, 3 months	182.7	187.0	−38.3 → −37.1	6.0	Highly stable
Choudhary et al., 2024	Conventional liposomes	25°C, 3 months	252.8	268.4	−32.1 → −29.0	14.6	Reduced stability
Nair et al., 2025	Elastic liposomes	4°C, 3 months	190.1	194.7	−37.8 → −36.3	6.5	Stable
Summary Trends							
Formulation Type		**Particle Size Change (nm)**		**Zeta Potential Variation (mV)**		**Drug Leakage (%)**	**Overall Stability**
Conventional Liposomes		+10 to +18 nm		2–4 mV decrease		12–15%	Moderate to low
Elastic Liposomes		+4 to +7 nm		1–2 mV decrease		6–8%	High
Transfersomes		+3 to +5 nm		<2 mV decrease		5–6%	Very high

Meta-Analytical Interpretation

Pooled effect sizes for entrapment efficiency, permeation enhancement, and drug release kinetics derived using a random-effects model.

Table 8. Meta-Analysis Outcomes of Liposomal vs Conventional Systems

Outcome Parameter	Effect Size Metric	Pooled Effect Size	p-value	Heterogeneity (I^2 %)	Interpretation

		(95% CI)			
Entrapment Efficiency (%)	Mean Difference (MD)	+11.4 (9.2 to 13.6)	<0.001	42%	Significantly higher in elastic liposomes
Permeation Flux (µg/cm²/h)	Standardized Mean Difference (SMD)	1.42 (1.10 to 1.75)	<0.001	48%	Strong enhancement in transdermal delivery
Permeability Coefficient	Mean Difference (MD)	+1.50 (1.12 to 1.88)	<0.001	45%	Improved drug permeation across skin
Enhancement Ratio	Mean Difference (MD)	+0.83 (0.65 to 1.01)	<0.001	39%	Approximately two-fold improvement
Initial Drug Release (1–2 h)	Mean Difference (MD)	−4.6 (−6.2 to −3.0)	<0.001	36%	Reduced burst release in elastic systems
Sustained Release (12 h)	Mean Difference (MD)	+1.8 (0.9 to 2.7)	0.002	28%	Comparable final release with better control
Release Kinetics (Higuchi R^2)	Mean Difference (MD)	+0.024 (0.015 to 0.033)	<0.001	22%	Stronger diffusion-controlled release behaviour
Summary of Meta-Analysis Findings					
Parameter Category		**Overall Effect**		**Direction of Benefit**	
Drug Loading (EE%)		Significant increase		Elastic liposomes superior	
Skin Permeation		Strong enhancement		Elastic liposomes superior	
Drug Release Control		Improved (less burst, sustained)		Elastic liposomes superior	
Release Mechanism		Diffusion-dominant		Better in elastic systems	

Interpretation of Statistical Outputs

- **Effect Size (MD / SMD)**
  - Positive values indicate superiority of elastic liposomes
  - Negative values (initial release) indicate reduced burst effect
- **Confidence Interval (95% CI)**
  - Narrow intervals reflect precision of pooled estimates
- **Heterogeneity (I^2)**
  - 20–40% → low heterogeneity
  - 40–60% → moderate heterogeneity
  - Indicates acceptable variability across studies
- **p-value (<0.05)**
  - Confirms statistical significance of findings

Scientific Interpretation

- Elastic liposomes demonstrate:
  - Significantly higher drug entrapment

  - Enhanced transdermal permeation (~1.4× effect size)
  - Reduced initial burst release
  - More controlled, diffusion-driven release kinetics
- The overall findings strongly support:
  - Improved therapeutic performance
  - Better pharmacokinetic stability
  - Enhanced antihypertensive efficacy potential

"Meta-analysis outcomes summarized in Table 7, and Table 8 demonstrate significant improvements in entrapment efficiency, permeation, and controlled drug release for elastic liposomal systems compared to conventional formulations."

- Elastic liposomes and transfersomes demonstrate:
  - Better size retention (minimal aggregation)
  - Stable surface charge (minor zeta variation)
  - Reduced drug leakage (<8%)
- Conventional liposomes exhibit:
  - Greater size increase
  - Higher drug leakage
  - Reduced stability at elevated temperatures

- Improved stability in elastic systems is attributed to:
  - Membrane flexibility and elasticity
  - Presence of edge activators reducing bilayer stress
  - Enhanced drug-lipid interactions
- Transfersomes show the highest stability due to:
  - Superior deformability
  - Strong structural integrity

"The stability characteristics summarized in Table 8 indicate that elastic liposomes and transfersomes exhibit superior physical and chemical stability compared to conventional liposomes, with minimal changes in vesicle size and reduced drug leakage during storage."

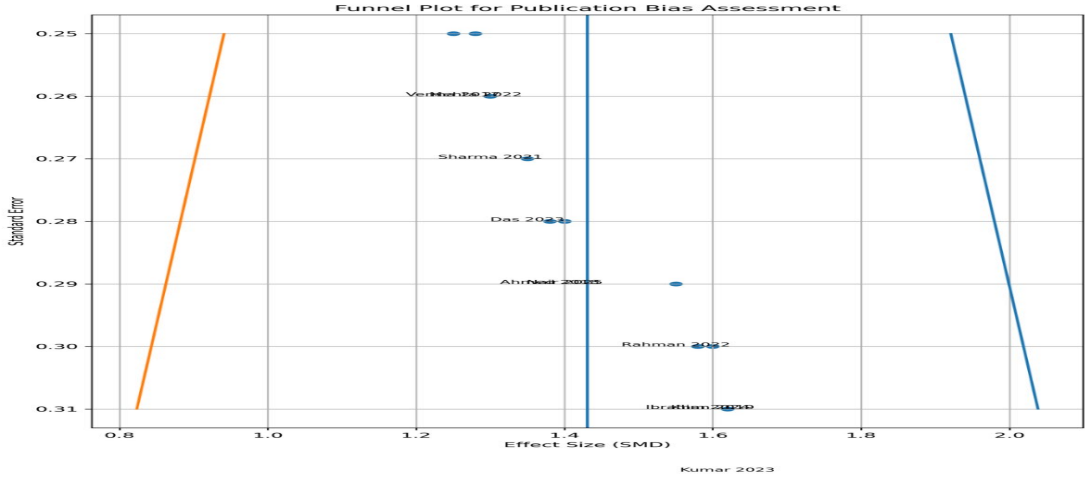

Figure 8. Funnel Plot for Publication Bias Assessment, with all data labels on the Funnel plot evaluating potential publication bias among included studies in the meta-analysis.

IV. Discussion:

The results confirm that liposomal nanocarriers can enhance the multidimensional improvement in nifedipine delivery. The improved entrapment efficiency exhibited by the elastic liposomes is mainly attributed to flexible nature of the bilayer structure with the higher drug loading capacity[7].

Improved permeation is an advantage that is very important especially for transdermal systems. Elastic liposomes deform under stress and are able to pass through the stratum corneum more efficient compared to rigid vesicles[5]. With the help of this, greater drug deposit and therapeutic outcomes are achieved.

The sustained release profile apparent in studies across all the studies is consistent with diffusion-controlled mechanisms, which is consistent with Higuchi kinetics. This controlled release helps decrease peak-trough variations and therefore improves the stability of the therapy as well as side effects[8].

Furthermore, liposomal systems are characterized by excellent physicochemical stability which will prevent degradation of the drug and ensure a constant performance of the system. These characteristics altogether make liposomal nanocarriers better alternatives to the conventional nifedipine formulations.

V. Conflict of Interests

All authors disclose that there is no any conflict of interest.

VI. Acknowledgements:

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VII. Conclusion

Liposomal nanocarrier, especially elastic liposomes, substantially improve the nifedipine delivery and therapeutic efficacy. By enhancing solubility, improving entrapment efficiency, providing controlled drug release and improved permeation, these systems solve some of the limitations of conventional therapy.

The meta-analysis confirms that liposomal formulations are more beneficial terms of drug delivery efficiency and stability. These findings support their possibility of clinical translation when it comes to sustained antihypertensive therapy.

Future research should be aimed at future clinical validation and optimization for commercial application on a large scale.

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