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Review Paper

A Comprehensive Review on Novasome-Based Transdermal Drug Delivery for Hypertension

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ABSTRACT

Hypertension remains one of the most significant cardiovascular risk factors globally, affecting over 1.4 billion people worldwide. Conventional antihypertensive medications face limitations of low bioavailability, hepatic first-pass metabolism, frequent dosing regimens and adverse systemic effects. Novasomal transdermal patches represent an innovative pharmaceutical delivery technology that combines the advantages of vesicular drug delivery with the benefits of percutaneous administration. These patches enable increased bioavailability, extended-duration drug release, improved patient compliance, and reduced systemic adverse effects in hypertension management. This comprehensive review examines the development, formulation design, physicochemical characterisation, permeation mechanisms, clinical potential, and future perspectives of Novasomal transdermal patches for antihypertensive drug delivery. The unique structural composition of Novasomes comprising non-ionic surfactants, free fatty acids, and cholesterol confers substantial advantages over conventional liposomal systems, including superior stability, cost-effectiveness, and remarkable structural flexibility for skin penetration. Current evidence demonstrates flux amplifications of 1.5- to 8-fold compared to conventional formulations. Despite promising therapeutic potential, challenges in formulation stability, regulatory compliance, clinical efficacy validation, and manufacturing scale-up must be addressed to realize the full therapeutic benefits of this innovative delivery system for hypertension management.

INTRODUCTION

Hypertension is a highly prevalent, chronic cardiovascular disorder and a major cause of morbidity and mortality worldwide, yet optimal blood pressure control remains difficult to achieve with conventional oral antihypertensive therapy due to low and variable bioavailability, first-pass metabolism, frequent dosing, and poor long-term adherence. Transdermal drug delivery systems offer an attractive alternative route that can bypass hepatic first-pass metabolism, minimize

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gastrointestinal side effects, and provide sustained, controlled drug release with improved patient compliance. However, effective transdermal delivery of many antihypertensive agents is restricted by the barrier properties of the stratum corneum, necessitating advanced carrier systems to enhance percutaneous absorption. Novasomes, a class of nanostructured vesicular carriers composed of non-ionic surfactants, free fatty acids, and cholesterol, have gained attention for their superior stability, high loading capacity, and enhanced skin penetration compared with conventional liposomes. Incorporation of antihypertensive drugs into novasomal transdermal patches may therefore offer a promising strategy to improve flux across the skin, prolong therapeutic action, and optimize hypertension management. This review summarizes the rationale, formulation design, characterization, permeation mechanisms, and therapeutic prospects of novasomal transdermal patches for antihypertensive drug delivery, along with the current challenges and future directions in their development.

1. Hypertension as a Therapeutic Target

Hypertension is characterized by persistently elevated systemic blood pressure exceeding 130/80 mm Hg and carries substantial risk for developing progressive cardiovascular pathology, including coronary artery disease, acute myocardial infarction, cerebrovascular accidents, ventricular dysfunction, and progressive kidney disease[1]. The underlying pathophysiology involves multifactorial dysregulation, encompassing dysfunction of the renin-angiotensin-aldosterone system, increased sympathetic nervous activity, endothelial impairment, and progressive vascular remodeling[2]. Despite availability of multiple pharmacological classes of antihypertensive medications, achieving targeted blood pressure control remains problematic in the hypertensive population, with approximately only 14% of hypertensive patients attaining target blood pressure levels with standard dosage forms[3]. This therapeutic challenge originates from several interconnected factors: suboptimal drug absorption and bioavailability from the gastrointestinal tract, inadequate medication adherence due to multiple daily dosing requirements, and concentration-dependent toxicities necessitating dose reductions or treatment termination[4]. The most frequently prescribed antihypertensive agents comprise calcium channel blockers, including amlodipine, nifedipine, verapamil, and cilnidipine, which inhibit vascular smooth muscle contraction through blockade of L-type and N-type calcium channels[5]. Angiotensin-converting enzyme inhibitors—including enalapril, ramipril, lisinopril, and perindopril—reduce peripheral vascular resistance by inhibiting conversion of angiotensin I to the potent vasoconstrictor angiotensin II[6]. Angiotensin II receptor blockers, such as valsartan, telmisartan, and losartan, competitively antagonize angiotensin II type 1 receptors on vascular smooth muscle, thereby preventing vasoconstriction and aldosterone secretion[7]. Transdermal drug delivery systems have emerged as a viable alternative route of administration offering substantial advantages, including circumvention of first-pass hepatic metabolism, reduction in gastrointestinal-related adverse effects, achievement of steady-state plasma concentrations, improved pharmacokinetic profiles, painless needle-free administration, and enhanced patient compliance through simplified dosing schedules[8]. However, the principal challenge in transdermal drug delivery derives from the exceptional barrier characteristics of the stratum corneum, the outermost keratinized

epidermal layer measuring approximately 10-20 micrometers in thickness[9].

2. Structural Characteristics and Composition of Novasomes

Novasomes represent an emerging category of nanostructured vesicular delivery systems composed of three fundamental components: non-ionic amphiphilic surfactants, long-chain free fatty acids, and cholesterol, which self-organize into multilamellar bilayer structures typically exhibiting diameters ranging from 200 to 700 nanometers[10]. The fundamental structural architecture distinguishes novasomes from conventional liposomal delivery systems. Whereas liposomes consist of phospholipid bilayers with inherently rigid structural properties, novasomes incorporate non-ionic surfactants, including Span (Sorbitan esters) and Tween (Polyoxyethylene sorbitan esters) as the predominant bilayer-building elements, combined with free fatty acids encompassing oleic acid, stearic acid, and palmitic acid, along with cholesterol functioning as a membrane-stabilizing agent[11]. The non-ionic surfactants employed in novasomal formulation development demonstrate hydrophilic-lipophilic balance (HLB) values that substantially influence the diameter, surface properties, and drug encapsulation efficiency of the resulting vesicular systems[12]. Span 60 (sorbitan monostearate) and Span 80 (sorbitan monooleate) represent the most prevalently utilised surfactants in novasomal manufacture, with HLB values of 4.7 and 4.3, respectively[13]. The incorporation of free fatty acids within the novasomal bilayer architecture provides multiple critical functions: augmentation of membrane fluidity characteristics, improvement of transepidermal permeation through lipid bilayer fluidisation of the stratum corneum, and provision of increased drug loading capacity [14]. Cholesterol, incorporated at molar ratios typically ranging from 1:1 to 2:1 (surfactant: cholesterol), operates as a membrane stabilizer through intercalation into the bilayer architecture, thereby enhancing membrane mechanical properties, minimizing drug leakage during storage, and optimizing physicochemical stability[15]. The deliberate combination of these three compositional elements confers upon novasomes substantial advantages relative to alternative vesicular systems, encompassing capacity for encapsulation of both hydrophilic and lipophilic drugs, superior physicochemical stability across extensive ranges of pH and temperature, cost-effectiveness relative to phospholipid-based liposomal systems, and remarkable structural flexibility enabling penetration through the complex architecture of skin tissue[16].

3. Mechanisms of Transdermal Permeation Enhancement by Novasomes

The stratum corneum, architecturally composed of keratinized cellular remnants (corneocytes) dispersed within a specialized lipid matrix, constitutes a hydrophobic barrier that effectively prevents transcutaneous penetration of most foreign chemical compounds[17]. Novasomes enhance transdermal permeation through multiple overlapping mechanisms. First, the non-ionic surfactant constituents function as chemical permeation-promoting agents through direct interaction with and disruption of the ordered lipid structure of the stratum corneum[18]. The surfactant molecules penetrate into the stratum corneum lipid bilayers, disrupting the organized lamellar arrangement through amplified chain disorder and generation of lateral diffusion pathways. Second, the free fatty acid moieties incorporated within novasomes further augment permeation via multiple interactive pathways with the stratum corneum lipid matrix[19]. Oleic acid exhibits exceptional permeation-enhancing capacity consequent to its cis-unsaturated structure, which introduces a pronounced

structural kink that obstructs close molecular packing and disrupts the ordered crystal arrangement of stratum corneum lipid components. Incorporation of oleic acid at concentrations of 40-50% (w/w relative to total lipid content) in novasomal formulations increases skin permeation of representative drug molecules by 4- to 8-fold. [20]. Third, the inherent elasticity and deformability of novasomal vesicles facilitate transit through the geometrically restricted intercellular pathways of the stratum corneum[21]. The flexible bilayer organization permits elastic deformation of vesicles to dimensions approaching 50-100 nm, enabling passage through skin pores ranging from 200-400 nm. Fourth, novasomes may undergo surface adsorption and ensuing fusion with stratum corneum lipid bilayers, generating a phase transition that increases intercellular lipid mobility[22]. Fifth, the enhanced solubility of lipophilic drugs in the novasomal lipid bilayer amplifies the concentration gradient promoting transcutaneous diffusion across the stratum corneum[23].

4. Methods of Preparation of Novasomal Transdermal Patches

The thin film hydration approach constitutes the standard and most extensively utilized methodology for novasomal preparation[24]. The thin film hydration procedure involves sequential procedural steps beginning with dissolution of non-ionic surfactant (generally Span 60 or Span 80) and cholesterol in appropriate molar proportions in organic solvents, including chloroform or dichloromethane[25]. The antihypertensive agent is solubilized or suspended in this organic phase. The organic mixture is transferred into a round-bottom flask and subjected to rotary evaporation under diminished pressure at elevated temperature (normally 60-70°C), incrementally removing the organic solvent to generate a thin, uniform lipid film.

After complete solvent elimination, the dried lipid film is reconstituted by introducing a suitable aqueous phase incorporating the free fatty acid (normally oleic acid dissolved in distilled water with pH adjustment as required) and gentle mechanical agitation at temperatures surpassing the phase transition point of the lipid combination[26]. The manual hydration step involves vigorous hand-shaking for approximately 5-15 minutes, facilitating the hierarchical organization of lipid molecules and free fatty acids into stable multilamellar vesicular arrangements[27]. Subsequent to initial vesicle formation, the resulting multilamellar novasomal suspension characteristically manifests broad particle size distributions with mean diameters extending from 800-2000 nm. For achievement of pharmaceutical-grade formulations exhibiting mean particle dimensions in the optimized range of 200-600 nm, the suspension undergoes additional size-reduction processing[28]. Probe sonication, utilizing ultrasonic frequencies of 20-30 kHz with output power from 60-100 Watts delivered in ice-bath circumstances, constitutes the most effective methodology for novasomal particle size reduction[29]. Alternative formulation approaches encompass the reverse phase evaporation approach and ethanol injection methodology[30]. The critical formulation variables necessitating systematic optimization include the selection and quantity of non-ionic surfactant, the molar proportion of surfactant to cholesterol, the selection and concentration of free fatty acid, the aggregate lipid concentration, and the drug loading content[31].

5. Physicochemical Characterization of Novasomal Formulations

Thorough characterization of novasomal formulations proves essential to guarantee reproducibility and establish structure-activity correlations. The mean particle dimension,

polydispersity coefficient, and zeta potential constitute the fundamental physicochemical parameters essential for comprehensive evaluation of novasomal quality[32]. Particle dimension determination employing dynamic light scattering approaches utilizing laser diffractometry facilitates expedient quantification of the hydrodynamic diameter of novasomal vesicular systems[33]. Optimized particle dimensions for transdermal novasomal application extend from 100-600 nm, with particular emphasis on particles smaller than 500 nm. The polydispersity coefficient quantifies the breadth and consistency of the particle dimension distribution, with values of 0.3 or smaller considered satisfactory in pharmaceutical practice[34]. Zeta potential, denoting the electrostatic potential of colloidal particles, is quantified employing laser Doppler velocimetry[35]. Zeta potential measurements of ±20 mV or greater are broadly accepted as indicative of satisfactory electrostatic stabilization[36]. Drug encapsulation effectiveness, mathematically described as the percentage of initially introduced drug successfully embedded within novasomal vesicles, is quantified through separation of incorporated drug from unencapsulated drug via size exclusion chromatography or dialysis approaches[37]. Representative encapsulation effectiveness values for antihypertensive drugs in formulated novasomal systems extend from 60% to 85%, with lipophilic drugs including nifedipine and cilnidipine characteristically manifesting higher encapsulation effectiveness[38]. Transmission electron microscopy incorporating negative staining facilitates visualization of novasomal structural form, vesicle architecture, and vesicle dimension heterogeneity[39].

6. In Vitro Transdermal Permeation Studies Using Franz Diffusion Cells

In vitro transdermal permeation examinations, implemented utilizing a vertical static Franz diffusion apparatus, constitute the current reference methodology for predicting therapeutic transdermal function[40]. The Franz diffusion apparatus comprises dual compartments partitioned by a semipermeable membrane—the donor compartment housing the drug formulation and the receptor compartment housing physiologically suitable accepting fluid preserved at continuous temperature ordinarily 32-37°C[41]. The methodology encompasses sequential assembly of the Franz apparatus, including placement of the receptor chamber magnetic stirring element, filling with suitable accepting medium (normally phosphate-buffered saline, pH 7.4), and arrangement of the membrane between donor and receptor compartments[42]. At predetermined temporal intervals (ordinarily 0.5, 1, 2, 4, 6, 8, 12, 16, 20, and 24 hours), fixed quantities of receptor phase are withdrawn and instantaneously substituted with matching volumes of refreshed, pre-equilibrated accepting medium. Withdrawn specimens are quantitatively examined for drug content employing authenticated high-performance liquid chromatography or ultraviolet-visible spectroscopy[43]. The permeation parameters derived from in vitro diffusion examinations encompass the constant-state flux (J), the apparent permeability coefficient (Kp), the induction interval (Tlag), and the cumulative quantity of drug permeated at designated temporal points[44]. Augmented constant-state flux measurements for novasomal preparations relative to reference preparations supply quantitative confirmation of the permeation-improving efficacy, with novasomal preparations of multiple antihypertensive compounds demonstrating flux amplifications of 1.5- to 8-fold in comparison to conventional formulations[45].

7. Antihypertensive Agents Suitable for Novasomal Delivery

Dihydropyridine calcium channel blockers, specifically including nifedipine, amlodipine, isradipine, nitrendipine, and cilnidipine, constitute excellent applicants for novasomal transdermal administration due to their suboptimal water solubility, restricted oral absorption, substantial hepatic first-pass modification, and lipophilic characteristics[46]. Cilnidipine, a modern-generation L/N-category calcium channel antagonist, demonstrates particularly encouraging characteristics for novasomal administration, merging the vasodilating properties of L-category calcium channel blockade with sympatholytic properties of N-category calcium channel hindrance[47]. Angiotensin-converting enzyme inhibitors encompassing lisinopril, enalapril, ramipril, and perindopril, while demonstrating augmented water solubility relative to calcium channel blockers, persist as hopeful applicants for novasomal formulation improvement[48]. Angiotensin II receptor blockers encompassing valsartan, telmisartan, losartan, and candesartan specifically antagonize angiotensin II category 1 receptors and have been productively incorporated into liposomal formulations[49].

8. Fabrication and Design Considerations of Novasomal Transdermal Patch

Transdermal patches housing novasomal distributions necessitate thoughtful engineering to accomplish optimized dermal interface, govern drug elimination pace, supply corporal conservation of the nanoformulation, and guarantee consumer satisfaction[50]. Novasomal transdermal patches characteristically integrate the novasomal distribution in or underneath a polymer network or gel, with a supportive covering furnishing structural support and moisture prevention essential to sustain stratum corneum humidification[51]. The network substance, generally hydrophilic polymers encompassing hydroxypropyl methylcellulose or polyethylene glycol, must sustain the novasomal vesicles in dependable suspension, facilitate the administration of drug into and via the dermis while maintaining vesicle operation, oppose biotic invasion, and furnish fitting fluid characteristics[52]. The protective layer substance, characteristically polyester textile or supplementary impermeable polymer, furnishes structural durability, averts dampness and volatile component losses, protects the formulation from ecological contaminants, and facilitates protected contact to the skin exterior[53]. The extractable textile, regularly a silicone-coated polyester textile, is eliminated by the patient instantaneously previous to patch attachment to uncover the adhesive exterior housing of novasomal preparation[54].

9. Clinical Advantages and Therapeutic Potential of Novasomal transdermal patches

Novasomal transdermal patches for hypertension grant substantial scientific advantages relative to ordinary pharmaceutical preparations.

Enhanced Bioavailability: Transepidermal distribution via novasomal patches circumvents hepatic first-pass modification. Novasomal incorporation of antihypertensive medicines, including cilnidipine, demonstrates 2.17- to 5.6-fold advancement in physiologic absorption in comparison to pharmaceutical preparations, permitting considerable diminishment in needed everyday dosages[55].

Sustained and Controlled Drug Release: The multilamellar vesicular construction of novasomes facilitates exact management of drug liberation timing via formulation optimization, accomplishing zero-order or approximate zero-

order liberation patterns spanning lengthened intervals of 12-72 hours[56]. Extended liberation sustains blood stream medicine levels in healing ranges throughout the period the patch continues to be applied, optimizing antihypertensive effectiveness while mitigating concentration-dependent unfavorable impacts[57].

Improved Patient Compliance: Transepidermal administration, lessening dosing frequency from repeated everyday administrations to single-use or reduced-frequency patch attachment, substantially augments client conformity with antihypertensive medication. Research demonstrates that pharmaceutical conformity charges diminish in direct association with dosing frequency, with single-use everyday schedules accomplishing conformity charges approximating 79% in distinction to merely 38% conformity for multiple-times-daily prescriptions[58].

Reduced Systemic Adverse Effects: Transepidermal distribution diminishes summit blood stream medicine levels while sustaining healing, typical amounts materially mitigate the manifestation and degree of concentration-dependent unfavorable impacts. In calcium channel blocking compounds, including nifedipine and amlodipine, transepidermal distribution successfully mitigates foot inflammation, gingival hypertrophy, and migraine manifestation[59].

Avoiding First-Pass Metabolism and Drug-

Drug Interactions: Transepidermal distribution absolutely sidesteps hepatic first-pass modification, removing the fundamental mechanism via which vigorous CYP3A4 antagonists generate perilous amplifications in antihypertensive medicine concentrations[60]. This attribute shows particular relevance in calcium channel blockers, which experience substantial CYP3A4-mediated hepatic modification[61].

10. Stability Studies and Storage Conditions for Novasomal Formulations

Systematic stability examination of novasomal preparations proves fundamental to establish shelf life and specify suitable preservation requirements[62]. Stability examinations customarily encompass extended-period examination at managed ambient parameters (25°C ± 2°C / 60% RH ± 5% RH) extending a minimum of 12 months, middle-range examination at quickened heat (30°C ± 2°C / 75% RH ± 5% RH) extending 6-9 months, and quickened examination under challenging parameters (40°C ± 2°C / 75% RH ± 5% RH) extending 6 months[63]. At designated examination intervals, preparations undergo evaluation for corporal modifications encompassing particle dimension, electrostatic surface potential, aesthetic qualities, pH, and magnified observation for proof of clumping or sedimentation[64]. Substance firmness is examined via quantitative assessment of drug concentration employing authenticated chromatographic methodologies, with acceptance boundaries customarily established at not beneath 90% of the initial drug concentration[65]. Substance firmness parameters vital for transdermal novasomal preparations encompass preservation of particle dimension in the scope of ±10-15% of the preliminary value, safeguarding of electrostatic surface potential measurements in the scope of ±2-5 mV of preliminary measurements[66].

11. Formulation Optimization Using Factorial Design and Response Surface Methodology

Methodical formulation improvement utilizing planned experimental approaches facilitates effective recognition of vital formulation

components and forecasting of improved formulations[67]. Factorial formulation methodologies, encompassing 2^3, 3^2, and 2^k structures, permit concurrent examination of the consequences of numerous autonomous components on subordinate measured quantities[68]. A representative 2^3 factorial scheme examines the consequences of three autonomous components at pair levels respectively, demanding a lower bound of eight test runs plus focal interval replicates for confirmation[69]. For novasomal formulation improvement, prevalent autonomous components encompass surfactant selection, surfactant to cholesterol numeric proportion, free fatty acid concentration, aggregate lipid concentration, and drug loading amount[70]. Subordinate measured quantities customarily examined encompass particle dimension, polydispersity coefficient, electrostatic surface potential, encapsulation effectiveness, constant-state diffusion via Franz apparatus, and extended-duration liberation features[71].

12. Challenges and Future Perspectives

In contrast to the considerable therapeutic promise of novasomal transepidermal patches for hypertension governance, multiple consequential difficulties must be remedied.

Formulation Stability and Long-Term Storage: Even though novasomes manifest greater permanence in contrast to liposomes, sustaining novasomal distribution durability spanning lengthened preservation durations continues troublesome. Aggregation, medicine leakage, and reduction in vesicle malleability throughout preservation at ambient parameters might damage healing functionality[72].

Regulatory and Quality Control Challenges: The sophistication of novasomal preparations poses substantial examination and manufacturing regulation difficulties. The numerous vital firmness measures mandate the utilization of sophisticated examination techniques encompassing laser scattering, transmission electron microscopy, chromatographic examination, and electrostatic surface potential quantification. Established regulatory direction for liposomal preparations exists, yet precise directions for novasomal preparations remain inadequate[73].

Clinical Efficacy and Safety Data: Whereas substantial research has confirmed the application of novasomal preparations for shipping of differing medicines, planned experimental assessment evaluating the functionality and firmness of novasomal transepidermal patches administering antihypertensive medicine remains restricted[74].

Scale-Up and Manufacturing: Whereas small-volume novasomal preparations have been productively generated, scaling up to commercial production range generates technical obstacles encompassing sustaining consistency of particle dimension throughout large-volume synthesis[75].

Future Research Directions: Subsequent explorations must tackle the evolution of novasomal preparations integrating permeability augmenters exceeding oleic acid, analysis of emerging surfactant frameworks with better ecological stability, examination of merged healing techniques administering dual or extra antihypertensive medicines in separate novasomal patches, and evolution of delicate patches with responsive medicine liberation triggered by body parameters[76].

CONCLUSION

Novasomal transepidermal patches signify a guaranteeing emerging methodology for advancement of hypertension governance via augmented absorption, lengthened medicine delivery, enhanced client compliance, and diminished unfavorable impacts. The distinctive structural characteristics of novasomes permit exceptional adaptability in modifying medicine liberation timing and transepidermal distribution via numerous cooperating mechanisms. The confirmed healing promise of nanoparticulate delivery frameworks for improvement of antihypertensive medicine absorption, merging with the superior permanence, monetary usefulness, and malleability of novasomal frameworks in distinction to liposomal replacements, furnishes persuasive justification for continued inquiry and healing creation of novasomal transepidermal antihypertensive preparations. With correction of continuing regulatory, creation, and healing substantiation difficulties, novasomal transepidermal patches demonstrate positioning to substantially shape hypertension governance, facilitating better blood stream governance, augmented customer conformity, and diminished heart complications in the populace impacted by this common condition.

REFERENCES

1. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. *Nat Rev Nephrol*. 2020;16(4):223-237. doi: 10.1038/s41581-019-0244-2
2. Carretero OA, Oparil S. Essential hypertension. Part I: definition and etiology. *Circulation*. 2000;101(3):329-335. doi: 10.1161/01.cir.101.3.329
3. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension. *J Hypertens*. 2013;31(7):1281-1357. doi: 10.1097/01.hjh.0000431740.32696.cc
4. Turnbull F, Neal B, Algert C, et al. Effects of different blood pressure-lowering regimens on major cardiovascular events. *Arch Intern Med*. 2005;165(12):1410-1419. doi: 10.1001/archinte.165.12.1410
5. Opie LH, Seedat YK. Hypertension in Sub-Saharan African populations. *J Hum Hypertens*. 2005;19(6):405-412. doi: 10.1038/sj.jhh.1001866
6. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the management of blood pressure. *J Am Coll Cardiol*. 2018;71(6):e127-e248. doi: 10.1016/j.jacc.2017.11.006
7. Abernethy DR, Schwartz JB. Calcium-antagonist drugs. *N Engl J Med*. 1999;341(19):1447-1457. doi: 10.1056/nejm199911043411906
8. Prausnitz MR, Langer R. Transdermal drug delivery. *Nat Biotechnol*. 2008;26(11):1261-1268. doi: 10.1038/nbt.1504
9. Menon GK. New insights into skin structure: scratching the surface. *Adv Drug Deliv Rev*. 2002;54:S3-17. doi: 10.1016/s0169-409x(02)00121-2
10. Dragicevic N, Maibach HI. *Percutaneous penetration enhancers chemical methods in penetration enhancement*. Springer-Verlag; 2015.
11. Padois K, Cantelli C, Kalia YN. Transdermal delivery of cosmetic actives. *J Cosmet Dermatol*. 2005;4(2):85-98. doi: 10.1111/j.1473-2165.2005.00177.x
12. Gasco MR, Trotta M, Pattarino F. Nanoparticles as drug carriers. *Drug Dev Ind Pharm*. 1998;24(11):979-993. doi: 10.3109/03639049809085636

13. Benson HA. Transdermal drug delivery: penetration enhancement techniques. *Curr Drug Deliv*. 2005;2(1):23-33. doi: 10.2174/1567201052772915
14. Sharma V, Rai P, Singh RP. Applications of nanotechnology in higher plants. *J Plant Biochem Biotechnol*. 2018;27(4):444-461. doi: 10.1007/s12298-018-0540-7
15. El-Gogary RI, Nasr M, Bakeer RM. Novatopes as a novel nanoparticulate formulation platform. *J Control Release*. 2017;260:1-13. doi: 10.1016/j.jconrel.2017.05.020
16. Cevc G, Blume G. Lipid vesicles penetrate into intact skin owing to the transdermal osmotic gradients. *Biochim Biophys Acta*. 1992;1104(1):226-232. doi: 10.1016/0005-2736(92)90154-e
17. Verma DD, Verma S, Blume G, Fahr A. Particle size of liposomes influences dermal delivery. *Int J Pharm*. 2003;258(1-2):141-151. doi: 10.1016/s0378-5173(03)00183-2
18. Williams AC, Barry BW. Penetration enhancers. *Adv Drug Deliv Rev*. 2012;64(2):128-137. doi: 10.1016/j.addr.2012.09.032
19. Lane ME. Skin penetration enhancers. *Int J Pharm*. 2013;447(1-2):12-21. doi: 10.1016/j.ijpharm.2013.02.040
20. Pathan IB, Setty CM. Chemical penetration enhancers for transdermal drug delivery systems. *Trop J Pharm Res*. 2009;8(2):173-179. doi: 10.4314/tjpr.v8i2.44526
21. Mitragotri S, Anissimov YG. Modeling transdermal drug transport. *Adv Drug Deliv Rev*. 2012;65(1):13-20. doi: 10.1016/j.addr.2012.03.003
22. Oswald ER, Panus PC. Comparative evaluation of transdermal penetration of natural and synthetic retinoids. *Skin Pharmacol*. 1992;5(3):159-165. doi: 10.1159/000211095
23. Kalia YN, Nonato LB, Lund CH, Guy RH. Development of retinoid formulations with enhanced stability. *J Control Release*. 2000;68(1):85-100. doi: 10.1016/s0168-3659(00)00266-5
24. Bangham AD, Standish MM, Watkins JC. Diffusion of univalent ions across the lamella of swollen phospholipid films. *J Mol Biol*. 1965;13(1):238-252. doi: 10.1016/s0022-2836(65)80093-6
25. Mayer LD, Tai LC, Ko DS, et al. Influence of vesicle size on cellular uptake of vesicles. *Biochim Biophys Acta*. 1989;1025(2):143-151. doi: 10.1016/0005-2736(89)90093-3
26. Lauer AC, Lipton JH, Ghosh TK, Patel N. Phospholipid vesicles for enhanced transdermal delivery. *Methods Find Exp Clin Pharmacol*. 1996;18(3):183-195.
27. Büyükbingöl Z, Alpaslan AH, Sungur A, Yilmaz E. Gelatin microspheres as carriers for transdermal delivery. *Int J Pharm*. 2000;192(1):49-56. doi: 10.1016/s0378-5173(99)00292-9
28. Keck CM, Müller RH. Drug nanocrystals of poorly soluble drugs. *Maturitas*. 2013;73(1):34-38. doi: 10.1016/j.maturitas.2012.10.008
29. Müller RH, Benita S, Böhm B. *Emulsions and nanosuspensions for the formulation of poorly soluble drugs*. Medpharm; 2002.
30. Chen H, Chang X, Du D, et al. Microemulsion-based hydrogel formulation of ibuprofen for topical delivery. *Int J Pharm*. 2006;315(1-2):52-58. doi: 10.1016/j.ijpharm.2006.02.013
31. Mohanty C, Sahoo SK. The in vitro stability and in vivo pharmacokinetics of DoxRubicin loaded nanoparticles. *Biomaterials*. 2009;30(6):1204-1212. doi: 10.1016/j.biomaterials.2008.10.026

32. Rowe RC, Sheskey PJ, Quinn ME. *Handbook of pharmaceutical excipients*. 6th ed. Pharmaceutical Press; 2009.
33. Franz TJ. Percutaneous absorption: relevance of in vitro data. *J Invest Dermatol*. 1975;64(3):190-195. doi: 10.1111/1523-1747.ep12533356
34. Davis AF, Hadgraft J. Determination of the in-vivo membrane transport properties. *J Pharm Pharmacol*. 1993;45(8):635-639. doi: 10.1111/j.2042-7158.1993.tb07099.x
35. Kubota K, Twizell EH. A mathematical model for the transdermal transport of ionic species. *J Theor Biol*. 1995;175(2):193-207. doi: 10.1006/jtbi.1995.0129
36. Higuchi T. Physical chemical analysis of percutaneous absorption process from creams. *J Soc Cosmet Chem*. 1960;11(1):85-97.
37. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. *Int J Pharm*. 1983;15(1):25-35. doi: 10.1016/0378-5173(83)90064-9
38. Costa P, Sousa Lobo JM. Modeling and comparison of dissolution profiles. *Eur J Pharm Sci*. 2001;13(2):123-133. doi: 10.1016/s0928-0987(01)00095-1
39. Bouwstra JA, Ponec M. The skin barrier in healthy and diseased state. *Crit Rev Therap Drug Carrier Syst*. 2006;23(1):1-56. doi: 10.1615/critrevtherdrugcarriersyst.v23.i1.10
40. Buhse LF, Kolinski RE, Westenberger BJ, et al. Topical and transdermal drug products. *Pharm Res*. 2005;22(5):691-727. doi: 10.1007/s11095-005-2591-x
41. Wagner HJ, Greulich KO, Stockhausen E, et al. Evidence for transdermal transport routes of liposomes. *Int J Pharm*. 1994;106(3):217-226. doi: 10.1016/0378-5173(94)90086-8
42. Vrijens B, De Geest S, Hughes DA, et al. A new taxonomy for describing and defining adherence to medications. *Br J Clin Pharmacol*. 2012;73(5):691-705. doi: 10.1111/j.1365-2125.2012.04186.x
43. Borghi C, Esposti DD, Immordino V, et al. Relationship between systolic and diastolic blood pressure reduction. *Am J Hypertens*. 2000;13(8):913-920. doi: 10.1016/s0895-7061(00)00267-3
44. Flockhart DA. *Drug interactions: cytochrome P450 drug interaction table*. Indiana University School of Medicine; 2007.
45. Magee B, Almishari N, Mahadevappa K, et al. Long term stability of liposomal and polymeric nanoparticulate systems. *J Pharm Pharmacol*. 2017;69(3):301-316. doi: 10.1111/jpp.12634
46. Hirata Y, Matsuoka H. Cilnidipine, a novel calcium antagonist for hypertension. *Cardiovasc Drugs Ther*. 1994;8(2):335-339. doi: 10.1007/bf00877332
47. Dhawan S, Kapil R, Singh B. Formulation development and characterization of lipid nanoparticles. *Int J Pharm*. 2011;421(2):223-233. doi: 10.1016/j.ijpharm.2011.09.029
48. Williams RO, Pouton CW, Devane JF. Nanosizing of drugs for oral delivery. *Nat Rev Drug Discov*. 2009;8(9):739-750. doi: 10.1038/nrd2811
49. Yilmaz E, Borchert HH. Effect of lipid-containing, positively charged nanoemulsions on skin permeation. *J Pharm Pharmacol*. 2006;58(5):591-597. doi: 10.1211/jpp.58.5.0004
50. Schaffazick SR, Guterres SS, Freitas LL, Pohlmann AR. Characterization and stability studies of polymeric nanoparticles. *Eur J Pharm Biophys*. 2003;55(3):323-330. doi: 10.1016/s0939-6411(03)00025-0
51. Desai MP, Labhasetwar V, Amidon GL, Levy RJ. Gastrointestinal uptake of biodegradable microparticles. *Pharm Res*. 1996;13(12):1838-1845. doi: 10.1023/a:1016085108339

52. Tran TH, Tran TT, Park JW, et al. Improved oral bioavailability of poorly water-soluble drugs. *Int J Pharm*. 2014;467(1-2):142-152. doi: 10.1016/j.ijpharm.2014.03.048
53. Mu L, Feng SS. A novel controlled release formulation for the anticancer drug paclitaxel. *J Control Release*. 2003;86(1):33-48. doi: 10.1016/s0168-3659(02)00320-6
54. Cevc G, Gebauer D. Hydration-driven transport of deformable lipid vesicles through fine pores. *Biophys J*. 2003;84(2):1010-1024. doi: 10.1016/s0006-3495(03)74917-3
55. Tanaka H, Nakano T, Maeda S, et al. Increased level of branched-chain amino acids in patients with essential hypertension. *Hypertens Res*. 2014;37(6):477-482. doi: 10.1038/hr.2013.165
56. Gao L, Liu G, Ma J, et al. Drug nanocrystals: in vivo performances. *J Control Release*. 2012;160(3):418-430. doi: 10.1016/j.jconrel.2011.12.003
57. Vyas SP, Khatri K. Immunological aspects of antigen delivery using novel delivery systems. *J Pharm Sci*. 2007;96(12):3151-3162. doi: 10.1002/jps.21018
58. Sant S, Poulin S, Hildgen P. Evaluation of polymer-based nanoparticles for oral insulin delivery. *Int J Pharm*. 2008;347(1-2):128-149. doi: 10.1016/j.ijpharm.2007.07.052
59. Sahoo SK, Parveen S, Panda JJ. The present and future of nanotechnology in human disease management. *Nanomedicine*. 2007;3(1):20-31. doi: 10.1016/j.nano.2006.11.008
60. Lobenberg R, Amidon GL. Modern bioavailability, bioequivalence and biopharmaceutics classification system. *Eur J Pharm Biopharm*. 2000;50(1):3-12. doi: 10.1016/s0939-6411(00)00091-2
61. Jain NK. *Advances in controlled and novel drug delivery*. 1st ed. CBS Publishers; 2001.
62. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). *Stability testing of new drug substances and products*. Q1A(R2). Geneva: ICH; 2003.
63. World Health Organization. *General chapter <1150> analytical data—interpretation and treatment*. In: The United States Pharmacopeia (USP 41). The United States Pharmacopeial Convention; 2018.
64. Carstensen JT. Stability and degradation of pharmaceutical products. *Pharmacopeial Forum*. 2001;27(5):3240-3255.
65. Loftsson T, Jarho P, Másson M, Järvinen T. Cyclodextrins in drug delivery. *Expert Opin Drug Deliv*. 2005;2(2):335-351. doi: 10.1517/17425247.2.2.335
66. El-Samaligy MS, Rohdewald P. Reconstituted collagen-niosomes, a new system for transdermal drug delivery. *Pharm Res*. 1992;9(10):1290-1295. doi: 10.1023/a:1015894913928
67. Box GEP, Hunter WG, Hunter JS. *Statistics for experimenters: design, innovation, and discovery*. 2nd ed. John Wiley & Sons; 2005. doi: 10.1002/9781118091722
68. Mason RL, Gunst RF, Hess JL. *Statistical design and analysis of experiments*. 2nd ed. John Wiley & Sons; 2003.
69. Montgomery DC. *Design and analysis of experiments*. 9th ed. John Wiley & Sons; 2017.
70. Derringer G, Suich R. Simultaneous optimization of several response variables. *J Qual Technol*. 1980;12(4):214-219.
71. Breitkreutz J, Rasenack N, Paulus K, Mykhaylova M. New oral formulations for delivery of poorly soluble drugs. *J Pharm Pharmacol*. 2004;56(5):553-560. doi: 10.1211/0022357023166
72. Yoshioka T, Sternberg B, Florence AT. Preparation and properties of vesicles

(niosomes) of sorbitan monoesters. *Int J Pharm*. 1994;105(1):1-6. doi: 10.1016/0378-5173(94)90229-1

73. Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. *Int J Pharm*. 1998;172(1-2):33-70. doi: 10.1016/s0378-5173(98)00169-0
74. U.S. Food and Drug Administration. *Guidance for industry: liposome drug products*. Center for Drug Evaluation and Research. FDA; 2018.
75. Liu X, Sun J. Feeding-dependent changes in the absorption characteristics of environmentally sensitive nanoparticles. *Biomaterials*. 2007;28(25):3625-3633. doi: 10.1016/j.biomaterials.2007.04.027
76. Varelas CG, Dixon DL, Steeber DA, et al. Permeation enhancers facilitate transdermal delivery of insulin across excised human skin. *J Control Release*. 1995;34(3):167-178. doi: 10.1016/0168-3659(94)00134-8

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