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Research Article

Comparative Pharmacokinetic Evaluation of Oral Anastrozole Suspension and Transdermal Nano-Spanlastics Patches in Albino Rabbits

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Abstract

Background: Anastrozole is a cornerstone in the treatment of estrogen receptor-positive breast cancer in postmenopausal women. Oral administration presents several challenges that can impact therapeutic efficacy and patient adherence. The adverse effects can potentially compromise treatment outcomes. ***Objective***: To compare the bioavailability of Anastrozole as a transdermal ANS-nano-spanlastics (SPLs) patch with oral ANS-suspension. ***Methods***: This study involved 12 female albino rabbits, weighing 2 kg, which were randomly divided into two groups of six animals each. Group I received a dose of 0.104 mg of pure anastrozole suspension orally, while Group II was administered Anastrozole as transdermal nano-Spanlastic patches. Plasma anastrozole concentrations were quantified using reverse-phase high-performance liquid chromatography (RP-HPLC). ***Results***: The results demonstrated significant differences between the oral and transdermal delivery of Anastrozole. For the oral suspension, the maximum plasma concentration was 38 ng/mL, achieved at 1.5 hours, with an AUC of 368 ng · h/mL. The nano-spanlastic patch produced a lower Cmax (24.2 ng/ml) at a delayed Tmax (24 hours) and a significantly greater AUC (10714.58 ng · h/ml). The relative bioavailability of the transdermal formulation was 29 times higher than that of the oral route after 120 hr. ***Conclusions***: The nanospanlastic transdermal patch offers a more efficient and sustained method of anastrozole delivery compared to conventional oral suspension.

Keywords: Anastrozole, Albino rabbits, Pharmacokinetics, Spanlastics, Transdermal patches.

التقييم الدوائي المقارن لتعليق الأناسترو زول الفموي والرقع النانوية الأمتدادية المرنة عبر الجلد في الأرانب البيضاء

الخلاصة

الخلفية: أناسترو زول هو حجر الزاوية في علاج سرطان الثدي الإيجابي لمستقبلات هرمون الاستروجين لدى النساء بعد انقطاع الطمث. يمثل الإعطاء عن طريق الفم العديد من التحديات التي يمكن أن تؤثر على الفعالية العلاجية والتزام المريض. يمكن أن تؤثر الآثار الضارة على نتائج العلاج. **الهدف**: مقارنة التوافر البيولوجي ل Anastrozole كرقعة ANS-nano-spanlastics عبر الجلد (SPLs) مع تعليق ANS عن طريق الفم. **الطرائق**: شملت هذه الدراسة 12 أنثى أرنب ابيض، تزن 2 كجم، تم تقسيمها عشوائيا إلى مجموعتين من ستة لكل منهما. تلقت المجموعة الأولى جرعة قدرها 0.104 مجم من معلق أناسترو زول النقي عن طريق الفم، بينما تم إعطاء المجموعة الثانية أناسترو زول كرقع نانوية مرنةعبر الجلد. تم قياس تركيزات أناسترو زول البلازما باستخدام الكروماتوغرافيا السائلة عالية الأداء في المرحلة العكسية (RP-HPLC). **النتائج**: أظهرت النتائج اختلافات ذات دلالة إحصائية بين التوصيل الفموي وعبر الجلد ل Anastrozole. بالنسبة للتعليق الفموي، كان الحد الأقصى لتركيز البلازما 38 نانوغرام / مل ، تم تحقيقه في 1.5 ساعة ، مع AUC 368 نانوغرام ساعة / مل. أنتجت الرقعة النانوية المرنة أقل Cماكس (24.2 نانوغرام / مل) في Tmax متأخر (24 ساعة) وAUC أكبر بكثير (10714.58 نانوغرام·ساعة / مل). كان التوافر البيولوجي النسبي للتركيبة عبر الجلد أعلى ب 29 مرة من الطريق الفموي بعد 120 ساعة. **الاستنتاجات**: توفر الرقعة عبر الجلد النانوية طريقة أكثر كفاءة واستدامة لتوصيل أناسترو زول مقارنة بالتعليق الفموي التقليدي.

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INTRODUCTION

Transdermal drug delivery systems (TDS) provide a convenient and effective approach for long-term administration of medications. The transdermal route functions by allowing drug molecules to diffuse through the layers of the skin, be absorbed into the dermal capillaries, and subsequently enter the systemic circulation [1]. One of the key benefits of TDS is its ability to bypass first-pass hepatic metabolism, thereby avoiding gastrointestinal side effects commonly associated with oral drug delivery [2]. Moreover, TDS ensures sustained and controlled release of the drug, leading to stable plasma concentrations over extended periods. By reducing dosing frequency and eliminating the discomfort associated with traditional methods, TDS significantly enhances patient adherence [3]. Additionally, drug delivery systems (DDSs) like patches act as reservoirs, enabling the controlled and sustained release of preloaded anticancer agents [4]. This regulated release profile reduces fluctuations in drug concentrations, thereby increasing tumor exposure to the therapeutic agents and ultimately enhancing the

overall efficacy of cancer treatment [5]. Introduced in 2011, the term "Spanlastic"—a fusion of *Span* and *Elastic*—marked a notable breakthrough in drug delivery systems. These nanoscale, amphiphilic vesicles are engineered using anionic surfactants combined with edge activators, resulting in superior stability and functionality when compared to conventional liposomes. Unlike liposomes, which are prone to oxidative degradation and variability in phospholipid composition, Spanlastics demonstrate enhanced resilience. Their bilayered architecture enables the efficient transport of both hydrophilic and lipophilic drugs across physiological barriers. This structure not only facilitates improved drug delivery but also protects active compounds from degradation in the biological environment, ultimately boosting their therapeutic effectiveness at the intended site of action [7]. Moreover, spanlastics exhibit osmotic activity and high chemical stability, which contributes to preserving the structural integrity of encapsulated drugs [8]. This stability is especially advantageous for prolonging systemic circulation time and facilitating sustained drug release, making spanlastics particularly suitable for long-term therapeutic applications [9]. Oral anastrozole, while effective in treating estrogen receptor-positive breast cancer in postmenopausal women, faces several limitations. These include poor aqueous solubility and extensive first-pass hepatic metabolism, both of which reduce its bioavailability and lead to variable drug levels. Additionally, patients often experience gastrointestinal side effects, musculoskeletal pain, and bone loss due to estrogen depletion. Its delayed absorption and fixed dosing further limit its clinical flexibility and effectiveness, especially in elderly or nutritionally compromised patients. These challenges underscore the need for enhanced delivery systems to improve therapeutic outcomes [11]. To overcome these challenges, the use of nanoparticle-based delivery systems is gaining increasing attention. These systems offer several advantages, including enhanced skin permeability, controlled and sustained drug release, and protection of sensitive drug molecules from degradation [12,13]. Plasma concentration-time profiles can be predicted using physiologically based pharmacokinetic (PBPK) models, which rely on the drug's physicochemical properties and physiological parameters. However, it is essential to validate these models using publicly available clinical pharmacokinetic data before their application [14,15]. Several studies have consistently shown that spanlastic vesicles significantly improve the transdermal delivery and systemic availability of drugs that suffer from low oral bioavailability due to poor solubility or extensive metabolism. These vesicles offer a non-invasive and effective alternative to oral administration, particularly for chronic conditions that require long-term therapy [7,9]. This study aims to compare the bioavailability characteristics of anastrozole administered via a transdermal ANS-nano-Spanlastics (SPLs) patch with those observed following oral administration of an ANS-suspension.

METHODS

Materials

Anastrozole was procured from Hyperchem for Chemicals (China). Absolute ethanol, HPLC-grade methanol, potassium dihydrogen phosphate (KH_2PO_4), and sodium hydroxide (NaOH) were obtained from Chem-Lab (Belgium). Letrezol was supplied by Bide Pharmaceutical Ltd. (China). Pioneer Co. provided Eudragit L-100, HPMC, and PEG 400 for Pharmaceutical Industries (Iraq).

Preparation of anastrozole nanospanlastics patch

A nano-Spanlastics dispersion of Anastrozole was prepared and optimized as outlined in Table 1.

Table 1: Composition of Anastrozole Nano-spanlastics patch

Ingredient	Amount
Anastrozole	0.104 mg as a nanospanlastics
Eudragit L-100	7.5 gm
HPMC	2.5 gm
PEG 400	1.5 ml
Ethanol	10 ml
DW	10 ml

Transdermal patches were formulated using the solvent-casting technique. Eudragit L-100 and HPMC were dissolved in 20 mL of ethanol and water and stirred thoroughly for 30 minutes using a magnetic stirrer set at 250 rpm at 70 °C. To this polymeric solution, 1.5 ml polyethene glycol 400 (PEG 400) was added as a plasticizer. Subsequently, 1 mL of anastrozole nano-Spanlastics was incorporated into the mixture (equivalent to 0.104 mg of Anastrozole, previously prepared using Span 60 and Tween 60 in a ratio of 7:3, with a sonication time of 5 minutes). The resulting solution was sonicated at 35 °C for 20 minutes to remove any entrapped air bubbles. The final formulation was cast onto Petri dishes pre-coated with a 5% w/v polyvinyl alcohol (PVA) backing layer. An inverted funnel was positioned over the dishes to regulate the evaporation rate, and the solvent was allowed to evaporate at room temperature for 24 hours [16].

In vivo pharmacokinetic study

A total of 12 female Albino rabbits, three months of age and weighing approximately 2 ± 0.015 kg, were used in this study. The animals were housed under standard laboratory conditions with free access to food and water throughout the experimental period. The in vivo experimental procedures were approved by the Research Ethics Committee for Experimental Investigations at the College of Pharmacy, University of Baghdad, Iraq, following protocol number REC03202417A.

Study design

Pharmacokinetic parameters were evaluated in twelve female albino rabbits following the ethical guidelines established by the National Committee for Research

Ethics in Science and Technology (NENT, Norway) [17]. The rabbits, approximately three months old, were randomly divided into two equal groups. As shown in Figure 1, Group I received an oral dose of 0.104 mg of pure ANS suspension. Group II was treated with an ANS nano-Spanlastics patch applied topically to a hairless area of the thoracic-abdominal region.

Figure 1: *In vivo* pharmacokinetic experiment.

To ensure proper contact and prevent loss of the patch, the application site was covered with a medical adhesive plaster. A single dose was administered to both groups, and comparative bioavailability was assessed based on serial blood sampling. Blood samples (2.0 mL) were collected from the marginal ear vein at predefined time intervals of 0.5, 1, 1.5, 5, 6, 10, 24, 48, 72, 96, and 120 hours post-administration. Samples were drawn into EDTA-treated tubes and immediately processed. Plasma was separated using centrifugation at 4500 rpm for 5 minutes (Hettich, Germany), then transferred into Eppendorf tubes and stored at −20°C until analysis [18,19]. A modified and validated reversed-phase high-performance liquid chromatography (RP-HPLC) method was employed to quantify ANS in plasma. The process was validated for linearity, specificity, precision, accuracy, lower limit of detection (LOD), lower limit of quantification (LOQ), and stability. The HPLC system (SYKAM, Germany) was equipped with a UV detector, a Phenomenex Luna C18 column (4.6 × 150 mm, 5 µm particle size), and a micro-volume double plunger pump (10 µL/stroke). The mobile phase consisted of 80% HPLC-grade methanol and 20% HPLC-grade water. The injection volume was 20 µL, with a flow rate of 1 mL/min. Detection was performed at a wavelength of 215 nm [20]. Pharmacokinetic parameters, such as maximum plasma concentration (Cmax), time to reach maximum concentration (Tmax), and the area under the plasma concentration-time curve from 0 to 120 hours (AUC 0-120), as well as extrapolated to infinity (AUC0-∞), were calculated. All calculations were conducted using PK-Solver® software [21].

Statistical analysis

The results are expressed as mean values ± standard deviation (SD) based on a sample size of three (n = 3). Statistical significance was determined at a threshold of $p < 0.05$. Comparative analysis of pharmacokinetic parameters, including Cmax, Tmax, and AUC 0-120, was performed using the Student's *t*-test [22,23].

RESULTS

As illustrated in Figure 2, a calibration curve was constructed using the proposed method for ANS-spiked plasma samples. The curve demonstrated excellent linearity over the 5 to 100 ppb concentration range, with a correlation coefficient (r^2) of 0.9999, indicating a strong linear relationship between concentration and response.

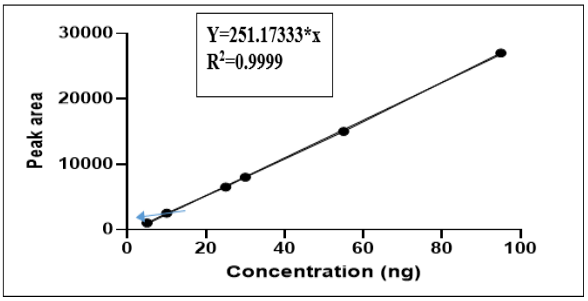

Figure 2: Calibration curve of plasma samples spiked with Anastrozole, using a mobile phase containing 10 ppb of Letrazole as the internal standard.

HPLC analysis confirmed that no endogenous plasma components interfered with the chromatographic detection, as evidenced by the blank plasma chromatogram shown in Figure 3, which exhibited no significant peaks at the retention times of the analytes.

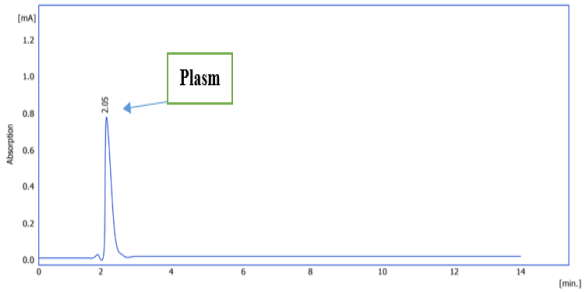

Figure 3: RP-HPLC chromatogram of blank plasma, showing no interference at the retention times of Anastrozole or the internal standard.

In the spiked plasma samples, anastrozole (ANS) and the internal standard, letrozole (LZ), were resolved, with retention times of 4.88 minutes and 8.08 minutes, respectively, as illustrated in Figure 4.

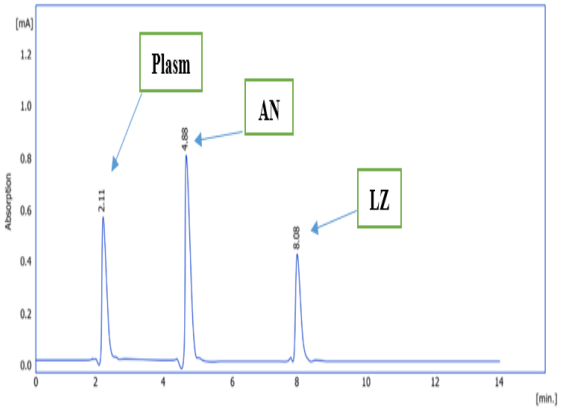

Figure 4: RP-HPLC chromatogram of a plasma sample spiked with ANS and the internal standard (LZ), showing distinct and well-separated peaks.

This separation indicates that no overlap or interference occurred between the analyte and the internal standard. The developed RP-HPLC method proved to be precise, specific, and sensitive for quantifying ANS in both mobile phase standard solutions and spiked plasma samples. All validation parameters were found to be within acceptable regulatory limits. The validated RP-HPLC method successfully identified Anastrozole (ANS) with a retention time of 4.88 minutes, confirming the method's reliability for quantitative analysis. A comparative bioavailability study was conducted to evaluate the pharmacokinetic performance of the ANS-loaded nano-Spanlastic patch versus the oral ANS suspension. Figure 5 presents the mean plasma concentration-time profiles for both the orally administered ANS suspension and the transdermal nano-Spanlastic patch, highlighting differences in absorption and systemic exposure.

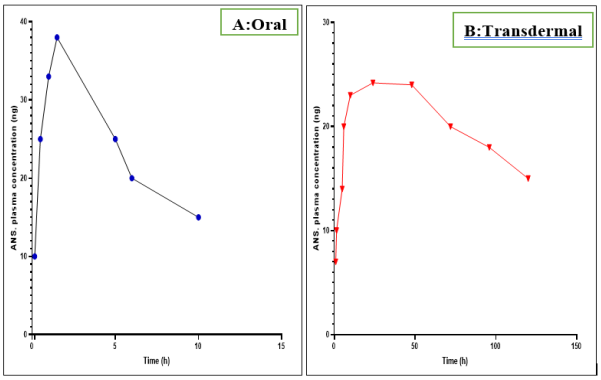

Figure 5: Mean plasma concentration-time profile of ANS following administration of a 0.104 mg dose via A: oral ANS suspension and B: transdermal ANS-loaded nano-Spanlastic patch.

In our study, we observed that ANS plasma concentrations in the transdermal formulation rose quickly and steadily during the first 24 hours. After reaching a peak (plateau), the levels then declined very slowly over the next two days. In the oral administration of Anastrozole (ANS), the peak plasma concentration was attained rapidly within 2 hours, followed by a swift and pronounced decline in drug levels thereafter. Table 2 presents the pharmacokinetic parameters obtained from oral and transdermal administration routes.

Table 2: Comparative Bioavailability Parameters of ANS: Transdermal Nano-Spanlastic Patch vs. Oral Pure Suspension

Pharmacokinetic parameters	Oral Pure Suspension	Transdermal Nano-Spanlastic Patch
Cmax (ng/ml)	38±0.2	24.2±0.04
Tmax (h)	1.5±0.01	24±0.01
AUC0-120 ng.h/ml	234.25±0.03	9028.99±0.16
$AUC_{0-\infty}$ ng.h/ml	368.25±0.01	10714.58±0.07

Values were expressed as mean±SD.

Each value represents the mean of triplicate measurements, and statistical significance was assessed using a Student's *t*-test. The results indicated that the maximum plasma concentration (C_{max}) and the time to reach it (T_{max}) were 38±0.2 ng/ml and 1.5±0.01 hours, respectively, for the oral ANS suspension and 24.2±0.04 ng/ml and 24±0.01 hours for the transdermal ANS nano-spanlastic patch. The differences in both Cmax and Tmax between the two delivery methods were statistically significant ($p< 0.05$), highlighting the enhanced absorption and prolonged release associated with the transdermal formulation.

DISCUSSION

The transdermal ANS-loaded nano-Spanlastic patch demonstrated significantly higher bioavailability compared to the orally administered ANS-free suspension. Notably, even though the Cmax for oral is higher than that for transdermal, the transdermal administration of Anastrozole (ANS) resulted in an approximately 29-fold increase in relative bioavailability compared to the oral route, as determined by comparing the area under the plasma concentration-time curve from time zero to infinity ($AUC_{0-\infty}$). This substantial enhancement reflects the improved systemic exposure of ANS when delivered transdermally, bypassing first-pass hepatic metabolism. Several key factors contributed to this enhancement: (i) Spanlastics are composed of non-ionic surfactants and edge activators, giving them elastic, ultra-deformable vesicle membranes. This elasticity enables them to squeeze through the narrow intercellular spaces of the stratum corneum (the outermost layer of the skin) and penetrate more deeply than rigid vesicles, such as conventional liposomes or free drug particles. (ii) the synergistic action of span and tween in enhancing skin permeability; (iii) the nanoscale particle size, large surface area, and deformability of the vesicles, which facilitate close contact with and penetration through the skin layers; and (iv) the ability of transdermal delivery to bypass hepatic first-pass metabolism, thereby preserving the drug's bioavailability, also allows Spanlastics to provide a lipophilic bilayer environment ideal for solubilizing poorly water-soluble drugs like Anastrozole. Our study demonstrated that the ANS compound exhibited a distinct signal at a retention time of 4.88 minutes, with no interference from the internal standard. This finding is consistent with the results reported by Sabareesh *et al*. (2024) [24]. Furthermore, the linearity of the analytical method was confirmed using six different concentrations, with a lower limit of quantification (LLOQ) established at 8 ng/mL, in agreement with the work of Al-Hashimi *et al*. (2024) [25]. The comparative analysis revealed a statistically significant difference between the tested formulations, consistent with similar findings reported in the literature [26]. The transdermal route offers several key advantages that contribute to the enhanced bioavailability of Anastrozole (ANS). Most notably, it enables the drug to bypass the hepatic first-pass effect by allowing direct absorption into the systemic circulation. Additionally, transdermal delivery ensures a controlled and sustained release of the drug, maintaining stable plasma concentrations over time. This approach reduces dosing frequency, minimizes fluctuations in drug levels, and helps mitigate side effects, ultimately improving patient compliance [27,28].

Conclusion

The developed Anastrozole (ANS)-loaded nano-Spanlastic transdermal patch exhibited significantly higher relative bioavailability compared to the orally administered ANS suspension. This suggests that Anastrozole is delivered into the bloodstream fairly rapidly at first and then maintains relatively stable concentrations over time, which is desirable for effective long-term treatment. This enhanced performance highlights the transdermal nano-Spanlastic patch as a more effective and patient-friendly alternative for ANS delivery. Given its ability to bypass hepatic first-pass metabolism and provide sustained drug release, the transdermal approach presents a promising strategy for improving ANS's pharmacokinetic profile. Future research may further establish transdermal delivery as a pivotal method for optimizing the therapeutic efficacy and bioavailability of Anastrozole.

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Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

REFERENCES

1. Ghaferi M, Alavi SE, Phan K, Maibach H, Mohammed Y. Transdermal drug delivery systems (TDDS): recent advances and failure modes. *Mol Pharm*. 2024;21(11):5373-5391. doi:10.1021/acs.molpharmaceut.4c00211.
2. Kumar V, Praveen N, Kewlani P, Arvind, Singh A, Gautam AK, et al. Transdermal drug delivery systems. In: Advanced Drug Delivery: Methods and Applications, Springer Nature Singapore; 2023 Oct 25 (pp. 333-362). doi: 10.1007/978-981-99-6564-9_13.
3. Wang L, Ma J, Li J, Fang L, Liu C. Transdermal patch based on pressure-sensitive adhesive: the importance of adhesion for efficient drug delivery. *Expert Opin Drug Deliv*. 2025;22(3):405-420. doi: 10.1080/17425247.2025.2460650.
4. Karve T, Dandekar A, Agrahari V, Peet MM, Banga AK, Doncel GF. Long-acting transdermal drug delivery formulations: Current developments and innovative pharmaceutical approaches. *Adv Drug Deliv Rev*. 2024:115326. doi: 10.1016/j.addr.2024.115326.
5. Martins M, Veiga F, Paiva-Santos AC, Pires PC. Drug repurposing and nanotechnology for topical skin cancer treatment: Redirecting toward targeted and synergistic antitumor effects. *ACS Pharmacol Transl Sci*. 2025;8(2):308-338. doi: 10.1021/acsptsci.4c00679.
6. Elnahas OS, Osama R, Abdel-Haleem KM, El-Nabarawi MA, Teaima MH, El-Sadek HM, et al. Integration of levofloxacin-loaded spanlastics and prednisolone into a buccal mucoadhesive sponge for combating severe pneumonia: In-vitro/ex-vivo assessment, qRT-PCR analysis, and quantification of the HMGB-1/NF-κB signalling pathway. *J Drug Deliv Sci Technol*. 2024;100:106019. doi: 10.1016/j.jddst.2024.106019.
7. Almohamady HI, Mortagi Y, Gad S, Zaitone S, Alshaman R, Alattar A, et al. Spanlastic nano-vesicles: A novel approach to improve the dissolution, bioavailability, and pharmacokinetic behavior of famotidine. *Pharmaceuticals*. 2024;17(12):1614. doi: 10.3390/ph17121614.
8. Ahmed Mousa S, Qelliny MR, Ibrahem RA, Hadiya S, Sarhan HA, Mady FM. Spanlastics: A unique formulation strategy in the delivery of pharmaceuticals-carbapenems as a model. *J Adv Biomed Pharm Sci*. 2024:117-125. doi: 10.21608/jabps.2024.298914.1221.
9. Bukhary HA, Hosny KM, Rizg WY, Alahmadi AA, Murshid SS, Alalmaie A, et al. Development, optimisation, in-vitro, and in-vivo evaluation of chitosan-inlayed nano-spanlastics encompassing lercanidipine HCl for enhancement of bioavailability. *J Drug Deliv Sci Technol*. 2024;96:105677. doi: 10.1016/j.jddst.2024.105677.
10. Dhilna F, Binitha RN, Riswina N, Divya S, Rima J, Janish PA, et al. Mechanisms of action for FDA-approved drugs targeting breast cancer. *J Senol Breast Dis*. 2025;38(1):100632. doi: 10.1016/j.senol.2024.100632.
11. Kim N, Lukong KE. Treating ER-positive breast cancer: a review of the current FDA-approved SERMs and SERDs and their mechanisms of action. *Oncol Rev*. 2025;19:1564642. doi: 10.3379/or.2025.1564642.
12. Ibrahim M, Fathalla Z, Fatease AA, Alamri AH, Abdelkader H. Breast cancer epidemiology, diagnostic barriers, and contemporary trends in breast nanotheranostics and mechanisms of targeting. *Expert Opin Drug Deliv*. 2024;21(12):1735-1754. doi: 10.1080/17425247.2024.2412823.
13. Nasrine A, Mohanto S, Narayana S, Ahmed MG. Enhanced pharmacokinetic approach for Anastrozole via macromolecule-based silk fibroin nanoparticles incorporated *in situ* injectables for oestrogen-positive breast cancer therapy. *J Drug Target*. 2025;33(5):793-803. doi: 10.1080/1061186X.2024.2449486.
14. Cao X, Li K, Wang J, Xie X, Sun L. PBPK model of pegylated liposomal doxorubicin to simultaneously predict the concentration-time profile of encapsulated and free doxorubicin in tissues. *Drug Deliv Transl Res*. 2025;15(4):1342-1362. doi: 10.1007/s13346-024-01680-0.
15. Bassani D, Parrott NJ, Manevski N, Zhang JD. Another string to your bow: machine learning prediction of the pharmacokinetic properties of small molecules. *Expert Opin Drug Discov*. 2024:1-6. doi: 10.1080/17460441.2024.2348157.
16. Suksaeree J, Maneewattanapinyo P, Panrat K, Pichayakorn W, Monton C. Solvent-cast polymeric films from pectin and Eudragit® NE 30D for transdermal drug delivery systems. *J Polymer Environ*. 2021;29:3174-3184. doi: 10.1007/s10924-021-02108-3.
17. National Committee for Research Ethics in Science and Technology. Guidelines For Research Ethics in Science and Technology. *JahrbWiss Eth*. 2009;14(1). Available at: https://www.forskningsetikk.no/en/guidelines/science-and-technology/guidelines-for-research-ethics-in-science-and-technology/
18. Jaiswal R, Wadetwar R. Tailoring cilnidipine nanostructured lipid carriers loaded transdermal patch for the treatment of hypertension: optimisation, ex vivo and in vivo studies. *J Dispers Sci Technol*. 2024:1-3. doi: 10.1080/01932691.2024.2431085.
19. Al-Zheery WH, Kassab HJ. Pharmacokinetic study of oral disulfiram suspension and topical transdermal nano-invasomes gel in Wistar rats. *Al-Rafidain J Med Sci*. 2024;7(1):159-163. doi: 10.54133/ajms.v7i1.1130.
20. El-Bakry R, Mahmoud DM, Attia ME, Fouad AG, Mohammed NH, Belal A, et al. Improving the targeting and therapeutic efficacy of anastrazole for the control of breast cancer: In vitro and in vivo characterisation. *Int J Pharm*. 2024;665:124684. doi: 10.1016/j.ijpharm.2024.124684.
21. Abbas IK, Abd Alhammid SN, Fadhil AA, Hareeja MM. Bioavailability of bilastine oral self-nanoemulsion: Comparative study with commercial formula in rats. *Al-Rafidain J Med Sci*. 2024;7(1):13-17. doi: 10.54133/ajms.v7i1.1024.

22. Hashim AA, Rajab NA. Anastrozole loaded nanostructured lipid carriers: Preparation and evaluation. *Iraqi J Pharm Sci*. 2021;30(2):185-195. doi: 10.31351/vol30iss2pp185-195.
23. Abdulqader AA, Rajab NA. Bioavailability study of posaconazole in rats after oral poloxamer P188 nano-micelles and oral posaconazole pure drug. *J Adv Pharm Edu Res*. 2023;13(2):141. doi: 10.51847/Q59uyvRmY3.
24. Sabareesh M, Rajangam J, Prakash Raj K, Yanadaiah JP. Formulation and evaluation of novel vesicular nanoethosomal patches for transdermal delivery of zidovudine: In vitro, ex vivo, and in vivo pharmacokinetic investigations. *J Dispers Sci Technol*. 2024:1-4. doi: 10.1080/01932691.2024.2444976.
25. Al-Hashimi NN, Shahin RO, El-Sheikh AH, Jibreel MJ, Alsakhen NA, Alqudah AM, et al. A new approach for determination of urinary 8-hydroxy-2′-deoxyguanosine in cancer patients using reinforced solid/liquid phase microextraction combined with HPLC-DAD. *Acta Chromatographica*. 2024;36(3):218-227. doi: 10.1556/1326.2023.01142.
26. Al-mansoori MK, Sabri LA. Preparation and evaluation of transdermal gel loaded with spanlastics containing meloxicam. *J Res Pharm*. 2024;28(4). doi: 10.29228/jrp.801.
27. Sulaiman HT, Rajab NA. Soluplus and solution HS-15 olmesartan medoxomil nanomicelle based oral fast dissolving film: in vitro and in vivo characterisation. *Farmacia*. 2024;72(4). doi: 10.31925/farmacia.2024.4.7.
28. Tawfik MA, Eltaweel MM, Fatouh AM, Shamsel-Din HA, Ibrahim AB. Brain targeting of zolmitriptan via transdermal threesomes: statistical optimisation and in vivo biodistribution study by 99mTc radiolabelling technique. *Drug Del Transl Res*. 2023:1-8. doi: 10.1007/s13346-023-01373-0.