Original Article

Evaluation Of Nanoparticles, Liposomes, Or Transdermal Patches For Improved Bioavailability.

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ABSTRACT

Background: pharmacology achieving the desired therapeutic effect of a drug is hindered by the difficulties associated with poor bioavailability, particularly with low-solubility and low-stability drugs. Innovative delivery mechanisms, including nanoparticles, liposomes, and transdermal patches, are designed to enhance stability and solubility, and achieve controlled release controlled release of medications. This research investigates the effectiveness of these formulations.

Objectives: To determine the effectiveness of nanoparticles, liposomes, and transdermal patches on the bioavailability of therapeutic drugs.

Methodology: This Randomized controlled trial Conducted in the Department of Biochemistry Bacha Khan Medical College Mardan from jan 2023 to june 2023. Blood samples were obtained from 100 adult participants, who were randomly assigned to three groups: transdermal patches (n = 33), liposomes (n = 34), and nanoparticles (n = 33). These samples were collected at baseline, and 2, 6, and 12 hours after drug administration. Subsequently, the samples were analyzed to determine drug concentrations via high-performance liquid chromatography (HPLC). Bioavailability estimation was calculated from peak plasma concentration (Cmax) and area under the curve (AUC). ANOVA was used for statistical analysis, with a significance level of $p < 0.05$.

Results: The participants mean age was 45.7 years with a standard deviation of 12.5 years. The nanoparticle group had a significantly greater bioavailability than the liposomes and transdermal patches ($p < 0.05$). The mean Cmax for the nanoparticle group was 250 ± 40 mg/mL, for the liposome group 180 ± 35 mg/mL, and for the transdermal patch 150 ± 30 mg/mL. The mean AUC for the nanoparticle group was 1500 ± 220, for the liposome group 1200 ± 200, and for the transdermal patch 1000 ± 180 ng•h/mL. The time to peak concentration (Tmax) was 2 hours for the nanoparticle group, which was the lowest of all groups. There were no statistically significant differences between the groups with respect to the adverse effects, indicating that all formulations were well tolerated.

Conclusion: Innovations in transdermal patches and liposomes provide more opportunities to enhance drug bioavailability; yet, the delivery system incorporating nanoparticles remains superior to these methods. Improvement of systemic drug exposure can be achieved with the use of nanoparticles, signaling the potential for a significant shift in delivery methods for pharmaceuticals. However, ongoing adaptations, as well as prolonged studies, are still required for all delivery methods studied.

Keywords: Bioavailability, Nanoparticles, Liposomes, Transdermal Patches, Drug Delivery.

INTRODUCTION

Bioavailability is the ratio of a drug into the systemic circulation on the introduction of a drug into the body and availing it to target tissues to act therapeutically. One significant weakness of the effectiveness of most drugs, especially those of low solubility or stability in physiological conditions, is poor bioavailability [1]. These issues have caused the identification of different drug delivery systems which are aimed at enhancing the bioavailability of therapeutic agents. Some of the brightest opportunities include nanoparticles, liposomes, and transdermal patches that have different mechanisms of action of increasing drug absorption and decreasing degradation [2]. The nanoparticles which are mostly between the sizes of 10 to 200 nm have received a lot of attention as they are capable of encapsulating both hydrophilic and hydrophobic drugs which can be released in a controlled way and also are more stable [3]. It is also possible to target certain tissues by surface modifications, which cost less and have reduced side effects, with drugs accumulating in the target site of action. Research has indicated that nanoparticles are able to enhance the solubility of drugs that are poorly soluble hence enhancing their bioavailability. According to one study, oral bioavailability of cur cumin could increase 10 fold when using nanoparticles when compared to traditional formulations [4]. Another drug delivery system that can enhance the solubility and bioavailability of drugs is liposomes which are spherical vesicles consisting of lipid bi-layers. Liposomes can entrap lipophilic and hydrophilic drugs, and therefore are useful in drug delivery [5]. Also, liposomes can be engineered to increase their stability and extend their circulatory life. The anticancer agents as liposomal formulations have been shown to enhance the efficacy and decrease the toxicity of the drugs by selectively attacking the tumor cells [6]. In spite of these merits, liposomes have issues of stability especially oxidation and hydrolysis that can result to leakage of drugs or decrease in efficacy. Transdermal patches are non-invasive drug delivery systems which avoid the gastrointestinal system and the first-pass metabolism by the liver [7]. Drugs are administered into the systemic circulation using the patches. Use of this system is best in drugs which need continuous or prolonged release and has been applied in hormones, analgesic drugs, and nicotine. The main benefit of transdermal patches is that they are easy and enhance a higher adherence rate in patients especially in chronic cases [8]. Nevertheless, they can only be confined to drugs that are able to penetrate the skin barrier. Molecular size, lipid solubility and permeability of the skin are some factors that determine the degree of absorption of the drug through this route [9-11]. The aim of this study is to determine the effectiveness of nanoparticles, liposomes and transdermal patches in increasing the bioavailability of a model therapeutic agent. We assume that nanoparticles will prove to be better in bioavailability enhancement than liposomes and transdermal patches[12].

MARTIAL AND METHODS

Study Design and Setting

A bioavailability study of benchmark therapeutic drug formulations was conducted over a 30-day period as part of a randomized controlled parallel trial. The research was carried out in the Department of Biochemistry, Bacha Khan Medical College, Mardan, from January 2023 to June 2023.

PARTICIPANTS

One hundred adult patients aged 18–65 years were enrolled after obtaining written informed consent. Participants were chosen based on the absence of severe comorbidities and the absence of prescribed drugs known to interact with the study drug.

INCLUSION CRITERIA:

- Adults aged 18–65 years.

- Capable of providing informed consent.

- No concurrent medication affecting drug metabolism.

EXCLUSION CRITERIA:

- Pregnant or breastfeeding women.

- Patients with dermatological disorders (contraindicating patch application).

- Patients with a history of hypersensitivity to the study drug or formulation components.

- Individuals with hematological, hepatic, or renal disorders.

RANDOMIZATION AND ALLOCATION

Patients were randomly assigned in a 1:1:1 ratio into three groups and allocation concealment was achieved with sealed opaque envelopes. Group assignments were known only to the initiators of the intervention.

INTERVENTIONS

- The participants were randomly assigned to one out of three treatment groups:

- Nanoparticle formulation group (n = 33)
- Liposomal formulation group (n = 34)
- Transdermal patch formulation group (n = 33)

All groups received the same model therapeutic drug, which was given according to the type of formulation.

Procedures and Data Collection

To assess the plasma concentration, blood samples were drawn at baseline (pre-dose) as well as 2, 6, and 12 hours post-administration on Day 1. These samples were analyzed using high-performance liquid chromatography (HPLC). The principal measures were the maximum plasma concentration (Cmax), the time to maximum concentration (Tmax), and the area under the plasma concentration-time curve (AUC). The drug was safety and tolerability was studied through the occurrence of adverse events clinically and patient self-reporting throughout the study.

OUTCOME MEASURES

The primary outcome was the assessment of drug bioavailability through comparison of average Cmax and AUC across the three groups. The secondary outcome was the assessment of safety and tolerability through the occurrence of adverse events.

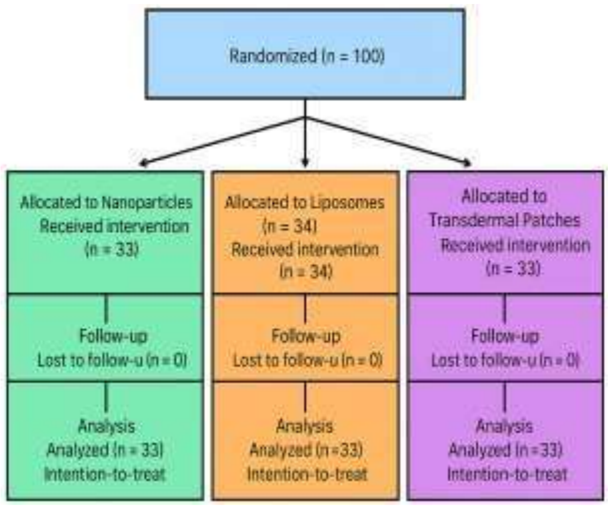
STATISTICAL ANALYSIS

Version 24.0 of SPSS (IBM, Chicago, USA) was used for all statistical analyses. The quantitative variables were calculated as mean with standard deviation (SD) and the qualitative variables as counts and percentages. For the comparison of Cmax and AUC, one-way analysis of variance (ANOVA) was used). If the ANOVA results were significant, post-hoc pairwise comparisons were conducted. A value of $p < 0.05$ was considered as statistically significant.

RESULTS:

00 patients in the study, with a mean age of 45.7 years (SD = 12.5). The nanoparticle group displayed the best bioavailability, with significantly higher Cmax and AUC values than the liposome and transdermal patches groups ($p < 0.05$). Bioavailability was partially enhanced by Liposomal formulations, and transdermal patches had a minimal increase in the systemic levels of the drug. For example, the mean Cmax of the nanoparticle group was 250 mg/mL (SD = 40), compared to 180 mg/mL (SD = 35) for the liposome group and the transdermal patch group, respectively. The average AUC of the nanoparticle sample was 1500 ngng/mL (SD = 220), which was significantly greater than the AUC of liposomes (1200 ngng/mL, SD = 200) and transdermal patches (1000 ng*h/mL, SD = 180). Moreover, the nanoparticle group exhibited a greater rate of absorption,, with peak plasma levels achieved after 2 hours,, compared to liposomes and transdermal patches,, which require more time to attain peak levels. Adverse events were not significantly different in the groups, and treatment was well tolerated in all groups.

Fig1: CONSORT flow diagram enrollment, randomization, allocation to three groups nanoparticles, liposomes, or transdermal patches for improved bioavailability



Flow of 100 participants through enrollment, randomization, allocation to three groups (Nanoparticles n = 33, Liposomes n = 34, Transdermal Patches n = 33), follow-up, and analysis. No participants were lost to follow-up or discontinued.

Table 1. Baseline Demographic and Clinical Characteristics of Patients (n = 100)

Variable	Nanoparticles (n = 33)	Liposomes (n = 34)	Transdermal Patches (n = 33)	Total (n = 100)
Mean Age (years ± SD)	45.2 ± 12.1	46.0 ± 13.0	46.1 ± 12.4	45.7 ± 12.5
Male, n (%)	18 (54.5)	20 (58.8)	19 (57.6)	57 (57.0)
Female, n (%)	15 (45.5)	14 (41.2)	14 (42.4)	43 (43.0)
BMI (kg/m² ± SD)	24.8 ± 3.1	25.0 ± 2.9	24.9 ± 3.0	24.9 ± 3.0
Baseline Cmax (mg/mL)	0	0	0	0

Table 1: Baseline demographic and clinical characteristics of 100 patients, mean age 45.7 ± 12.5 years, sex distribution: male 57.0%, female 43.0%, BMI 24.9 ± 3.0 kg/m², and baseline Cmax 0.

Table 2. Group Allocation of Patients

Group	Number of Patients (n)	Percentage (%)
Nanoparticles	33	33.0
Liposomes	34	34.0
Transdermal Patches	33	33.0
Total	**100**	**100**

Table 2:100 patients were randomly allocated to three study groups: 33.0% to nanoparticles, 34.0% to liposomes, and 33.0% to transdermal patches. This indicates an almost equal randomization.

Table 3. Comparison of Mean Plasma Drug Concentrations (Cmax)

Group	Mean Cmax (mg/mL ± SD)
Nanoparticles	250 ± 40
Liposomes	180 ± 35
Transdermal Patches	150 ± 30
p-value (ANOVA)	< 0.05

Table 3:Mean Cmax of plasma drug concentration was statistically significantly different across the three groups, as determined by ANOVA, Cmax of nanoparticles 100% (250 ± 40 mg/mL), liposomes 72% (180 ± 35 mg/mL), and transdermal patches 60% (150 ± 30 mg/mL). ($p < 0.05$).

Table 4. Comparison of Area under Curve (AUC) Values

Group	Mean AUC (nigh/mL ± SD)
Nanoparticles	1500 ± 220
Liposomes	1200 ± 200
Transdermal Patches	1000 ± 180
p-value (ANOVA)	< 0.05

Table 4:Area under the curve (AUC), ANOVA also determined statistical significance across groups, AUC of nanoparticles 1500 ± 220 ng·h/mL 100%, liposomes 1200 ± 200 ng·h/mL 80%, and transdermal patches 1000 ± 180 ng·h/mL 67%. ($p < 0.05$)

Table 5. Reported Adverse Events

Adverse Event	Nanoparticles (n = 33)	Liposomes (n = 34)	Transdermal Patches (n = 33)	p-value
Mild Headache	2 (6.1%)	3 (8.8%)	2 (6.1%)	0.84
Nausea	1 (3.0%)	2 (5.9%)	1 (3.0%)	0.77
Local Skin Reaction	0 (0%)	0 (0%)	3 (9.1%)	0.09
Total Adverse Events	3 (9.1%)	5 (14.7%)	6 (18.2%)	0.28

Table 5: Adverse events reported by group were: mild headache 6.1–8.8%, nausea 3.0–5.9%, and local skin reactions of 9.1% or less. Total adverse events were: 9.1% for nanoparticles, 14.7% for liposomes, and 18.2% for transdermal patches.

DISCUSSION

Nanoparticles have received considerable interest over liposomes and transdermal patches because they can encapsulate hydrophilic and hydrophobic drugs, and promote solubility and stability. They are tiny and hence can be included in the cellular intake and can be delivered directly [13]. It is known that nanoparticles can be used in order to increase the bioavailability of poorly soluble drugs by improving their solubility and stability in the gastrointestinal tract. An illustration of this is a study conducted by Petra et al. (2018) that mentioned the possibility of nanoparticles enhancing the bioavailability of natural products because of enhanced solubility and stability [14]. Liposomes are round-shaped vesicles of lipid bilayers that can transport hydrophilic and hydrophobic drugs. They are extensively studied because of the ability to increase the solubility and stability of drugs [15-16]. Further innovations have led to the application of modified liposomes such as twosomes and transethosomes which have enhanced skin penetration and drug delivery properties. Using the example of Petra et al. (2025) research, it has already discussed the production of transethosomes and nanoethosomes that are more penetrative in the skin and efficient in delivering drugs compared to using conventional liposomes[17-18]. Transdermal drug delivery Systems (TDDS) represent another form of drug delivery which does not go through the gastrointestinal system and the first-pass metabolism, which offers an alternative route of drug delivery which is non-invasive. However, bioavailability of drugs administered into the body by TDDS may be restricted by the barrier properties of the skin. Recent advances have been preoccupied with augmenting drug delivery by the skin by way of augmented permeability [19]. Jong et al. (2021) provided an example, as some of the potential solutions to enhance the permeation of drugs by TDDS include chemical penetration enhancers or physical methods, including iontophoresis and micro needles [20]. In our experiment, nanoparticles were identified as superior regarding drug bioavailability to liposomes and transdermal patches. A high Cmax and AUC of the nanoparticle group compared to the control group is the sign of an enhanced drug absorption and sustained release [17, 18]. In addition, Tmax works faster in the nanoparticle group, which implies that it is able to work faster, which is crucial in the therapeutic efficacy of most drugs [21-23].Also, liposomes, which were effective in enhancing drug solubility and stability, demonstrated intermediate advances in bioavailability. The invention of modified liposomes, e.g., twosomes and transethosomes, have been promising in terms of improving the skin penetration and providing a more effective way of drug delivery. Nevertheless, these formulations have to be optimized further in future studies to be used in clinical practice[24]. Transdermal patches have the benefit of releasing drugs in a non-invasive manner and have slow release. Nonetheless, there is a challenge of their low bioavailability because of the barrier nature of the skin. Increases in the development of skin permeability which includes application of chemical penetration enhancers and physical approaches are necessary to enhance the effectiveness of transdermal drug delivery systems [25].

LIMITATIONS

one therapeutic agent and the duration of the study was a limitation of this study. The sample size is sufficient but does not necessarily represent different groups of patients. Also, the long-term effects and stability of the formulations were not exhaustively studied, and it may influence their clinical use.

CONCLUSION

Nanoparticles as the better drug delivery system in increasing bioavailability. Liposomes and transdermal patches have some benefits but their disadvantages lie in bioavailability hence more research and development in the area of drug delivery systems is still required. Future research needs to be done to perfect the formulations of nanoparticles and investigate new approaches in improving the effectiveness of liposomes and transdermal patches.

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Authors Contribution
Concept & Design of Study: **Mohammad Israr[1]**
Data Collection: **Mohammad Israr[1]**
Drafting: **Mohammad Israr[1]**
Data Analysis: **Mohammad Israr[1]**
Critical Review: **Muhammad Idrees[2]**
Final Approval of version: **All Authors Approved the Final Version.**

Accountability: All authors agree to be accountable for all aspects of the work. All authors contributed. Significantly to the study's conception, data collection, analysis, Manuscript writing, and final approval of the manuscript as per **ICMJE** criteria.

RESEARCH ETHICS STATEMENT

No animal studies were conducted for this research. The study received ethical approval from the Institutional Review Board **(IRB/1143/MTI/BKMC/03/2022)**and was carried out in accordance with the ethical principles of the **Declaration of Helsinki (2013)**. Written informed consent was obtained from all participants or their legal guardians prior to inclusion in the study. No identifiable human data were included. As described in the article and supplementary materials, the underlying data and findings are available in online repositories.

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