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Development of Novel Drug Delivery Systems for Enhancing the Bioavailability of Poorly Soluble Drugs

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Abstract - One of the most effective ways to solve issues with medication bioavailability is via the use of novel drug delivery systems (NDDS). It refers to how quickly and to what degree a medicine reaches its intended target following delivery. Since only a tiny percentage of the dose actually makes it into the bloodstream and reaches the intended target, most modern medications have low bioavailability and need greater dosages. A large quantity of medication is wasted and unwanted side effects occur as a consequence of this. The primary goal of pharmaceutical technology is to increase the bioavailability of medications by making them more soluble and permeable. The idea behind NDDS is nanotechnology, which allows for the decrease in medication particle weight while simultaneously increasing stability and enhancing functioning. This review looks at the many methods for increasing bioavailability and the pros and cons of each.

Keywords: Bioavailability, Solubilization, chemical modifications, Novel Drug Delivery Systems; Solubility

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INTRODUCTION

To lessen the medicine's influence on vital tissues and undesirable side effects, as well as to increase its bioavailability, new drug delivery methods are being developed. Because of this, medicinal chemicals are able to accumulate at the site of action more effectively, which in turn reduces the dosage of the drug needed at a predetermined rate. The remarkable potential of nanoparticles, which are structures less than 100 nm in size, as carriers of drugs has been recently shown by advancements in nanotechnology. Because of their tiny size, these nanostructures have exceptional physicochemical and biological characteristics that make them useful in biomedicine. These characteristics include, but are not limited to, an increased reactive area and the capacity to penetrate cell and tissue barriers. Because of their very high surface-to-volume ratio, nanoparticles dissolve more quickly in solutions, increasing bioavailability while decreasing toxicity and requiring lesser dosages of medication. Oral and intravascular drug delivery systems typically disperse therapeutic molecules throughout the body via the systemic blood circulation, increasing the likelihood that some of these molecules may not reach their intended targets and instead accumulate in the blood, where they can cause unwanted side effects. Because of their insolubility in water, short plasma half-life, low serum stability, and possible immunogenicity, the medicinal and therapeutic molecules are quickly cleared out of the mononuclear phagocytic system (MPS), reducing their efficacy. A drug's or metabolite's bioavailability is its ability to reach its target location in the body and how quickly it does so after entering the bloodstream.

The non-dispersible drug delivery systems (NDDS) such as liposomes, niosomes, bilosomes, phytosomes, etc., which avoid the side effects of medications accumulating in unintended places and enhance the dispersion of macrophages in both young and old patients. Benefits include enhanced solubility, permeability, stability, and prolonged administration, as well as protection against physical and chemical deterioration. Oral administration of lipophilic medicines becomes the limiting step in their rate of breakdown and absorption. the Biopharmaceutics Classification System (BCS) provides a clear explanation for the solubility and intestinal permeability of drugs that are absorbed by the intestinal wall. This review article focuses on many innovative drug delivery technologies that may improve the bioavailability of medications that are not highly soluble.

In order to create a uniform system, solubility—the ability of a solute to dissolve in a solvent—is crucial.

One way to put it quantitatively is that solubility is the necessary solute strength in a solution at a certain temperature, pressure, and pH. Solubility, on the other hand, refers to a material's qualitative melting point in a saturated solution. Various terms are used to describe solubility, including molality, volume fraction, percentage, parts of solvent, molarity, mole fraction, and many more. A solubility measurement in milliliters of solvent is required to dissolve one gram of a solute, according to the US Pharmacopoeia. There are two common methods for determining solubility: thermodynamic and kinetic. The key difference between the two approaches is that thermodynamic solubility tests employ a solid chemical introduced to an aqueous media, while kinetic solubility tests use a pre-dissolved molecule as the starting material. If you want to know, "How much does the substance dissolve?" thermodynamic solubility is the answer. When asked, "How much does the molecule precipitate?" kinetic solubility provides the opposite response. When determining the solubility of medications that are weakly soluble, thermodynamic solubility clearly plays a crucial role. Thermodynamic solubility also plays a role in the dissolving process. There is a difference between solubility and dissolution, which should be noted. "Dissolution" is employed when a gas, liquid, or solid solute becomes a solution by dissolving it in a solvent.

LITERATURE REVIEW

Sushmitha, A. & Balaji, A. & UmaShankar, M.S. (2013). The term "bioavailability" refers to the amount and rate of unmodified medication absorption into the bloodstream from its dose form. When a medicine has issues with water solubility, sluggish dissolving rate in biological fluids, stability of drug dissolved at physiological pH, bio membrane permeability, and substantial presystemic metabolism, it is said to have poor bioavailability. Because of its many advantages, including low cost, high patient compliance, few sterility requirements, and the freedom to build a dosage form that suits the patient's needs, oral ingestion is the most popular and practical method of drug delivery. This has led several generic pharmaceutical businesses to focus on making oral medication formulations that are bioequivalent. The low bioavailability of formulation components with GRAS status is one of the obstacles in developing micro emulsions, self-emulsifying drug delivery systems. The most crucial aspect of drug formulation development is ensuring the medication's bioavailability, as this determines both the drug's formulation and its therapeutic effectiveness.

Mehta, Abhinav & Jain, Neha & Grobler, Anne & Bharti, Vandana. (2016). One of the most effective ways to solve issues with medication bioavailability is via the use of novel drug delivery systems (NDDS). Definition: the time it takes for a medicine to reach its intended target after administration. Since only a tiny percentage of the dose actually enters the target location after administration, most modern medications have low bioavailability and need greater dosages. Because of this, a lot of medication is wasted and bad things happen. The primary goal of pharmaceutical technology is to increase the bioavailability of medications by making them more soluble and permeable. A key component of NDDS is nanotechnology, which allows for the decrease in drug particle weight while simultaneously increasing stability and enhancing functioning. The many methods for increasing bioavailability and the pros and cons of each are the subject of this review.

Gowthami, Buduru & Krishna, S.V. & Rao, D. (2020). There are a number of advantages to oral administration that make it the most popular and practical method of delivery. However, creating an effective formulation is mostly concerned with issues like inadequate solubility or enzymatic/metabolic activity. The majority of the new medicine compounds under development are hydrophobic, and over 40% of the pharmaceuticals on the market are hydrophobic as well. Nanotechnology is one of the methods that have been proposed to address the difficulty of creating medications that are insoluble in water. Nanocarriers and technologies that have improved the bioavailability of medications with low solubility are the focus of this study.

Dey, Sanjay & Jha, Sajal & Malakar, Jadupati & Gangopadhyay, Dr. (2012). Many people are interested in the self-emulsifying drug delivery system (SEDDS) because it can increase the oral bioavailability of drugs that aren't particularly soluble or absorbed. The components of SEDDS are oils, co-surfactants, and surfactants. Under the right conditions light stirring and digestive motility it gets emulsified when it comes into touch with an aqueous solution of the GIT. Since SEDDS come in a variety of dosage forms they may self-emulsify to enhance the oral absorption of sparingly soluble medicines. Among the most difficult aspects of medication formulation is increasing the bio-availability of medicines having these characteristics. Many drug delivery system technologies, solid dispersions, micronization, and cyclodextrines complex formation are detailed in published works. One method that has recently attracted a lot of interest for improving oral bio-availability while reducing dosage is the self-emulsifying drug delivery system (SEDDS). The components of SEDDS—oil, surfactants, solvents, and cosolvents/surfactants—are all in an isotropic mixture. To increase the pace and extent of oral absorption, SEDDS might be a potential method for lipophilic medicines with dissolution rate-limited absorption.

Rashid,et.al. (2019). A drug's bioavailability is one of its primary pharmacokinetic characteristics; it is the percentage of a dosage that enters the bloodstream unmodified that is used to indicate the drug's systemic availability. In order to prove that the medicine achieves the desired systemic exposure for successful treatment, bioavailability testing is essential. The concept of bioavailability has grown in significance in the field of drug development and

discovery in the last few years. A thorough literature study has been conducted on the topic of bioavailability and methods for improving it, with an exclusive emphasis on more recent publications. Databases such as PubMed, Science Direct, and generic Google searches were used for data mining. The acquired data was thoroughly examined and described in a generalized way. The primary goal of this review was to compile all the current methods and their pharmaceutical uses for enhancing the bioavailability of poorly water-soluble drugs by addressing stability issues, physicochemical properties, and mechanical properties. Various novel approaches have been developed to improve the bioavailability of medications that are not easily absorbed by the body. These include formulations based on nanotechnology, bio-enhancers, solid dispersions, and lipid and polymer-based formulations, among many others. The pharmaceutical industry's need for innovative, more effective methodologies in pharmaceutical science to develop various dosage forms with enough systemic availability and improved patient compliance has been greatly impacted by these strategies, although further research is still required.

RESEARCH METHODOLOGY

This methodology involved the design, preparation, and evaluation of NDDS formulations such as nanoemulsions, nanocrystals, and liposomes using a methodical experimental strategy, researchers investigated the possibility of developing new drug delivery systems (NDDS) to increase the bioavailability of medications with low solubility. Each stage of the study was carefully planned to address specific aspects, including solubility enhancement, particle size reduction, drug release profiles, bioavailability, stability, and safety.

Drug Selection and Preparation

The study focused on poorly soluble drugs, selected based on their therapeutic relevance and low aqueous solubility. Examples include Curcumin, Itraconazole, and Nifedipine. The pharmaceuticals were integrated into different NDDS by means of cutting-edge procedures as thin-film hydration for liposomes, ultrasonic emulsification for nanoemulsions, and high-pressure homogenization for nanocrystals. The formulations were optimized by varying process parameters to achieve desired characteristics.

Characterization of NDDS

Comprehensive physicochemical characterization was performed to evaluate the quality and performance of the NDDS:

1. Solubility Studies: Solubility enhancement was assessed by comparing the drug's solubility in its pure form and in the NDDS formulations.

2. Particle Size Analysis: Dynamic light scattering (DLS) was employed to determine particle size, polydispersity index (PDI), and zeta potential, ensuring uniformity and stability of the formulations.

3. In-vitro Drug Release: The rate and amount of medication release over time were determined by evaluating drug release profiles using a USP dissolving device.

Bioavailability Studies

The pharmacokinetic performance of the NDDS formulations was assessed in animal models. In order to assess the improvement in bioavailability, we assessed Kmax, Tmax, and AUC, which stand for maximum plasma concentration and area under the curve, respectively. These results were compared with the pharmacokinetic data of the pure drug.

Stability Studies

Using accelerated settings, the formulations' stability was assessed over a six-month period. The stability of the formulations was evaluated during storage by routinely monitoring parameters such drug concentration, particle size, and zeta potential.

Toxicity Evaluation

Safety studies were conducted using animal models to determine the toxicity profile of the NDDS formulations. Dose-dependent toxicity was analyzed to identify any adverse effects and ensure the formulations were safe for use.

DATA ANALYSIS

Table 1: Solubility Data of Poorly Soluble Drug

Drug Name	Pure Drug Solubility (mg/mL)	NDDS Solubility (mg/mL)	Fold Increase
Curcumin	0.01	0.35	35x
Itraconazole	0.05	0.75	15x
Nifedipine	0.10	1.20	12x

The solubility of poorly soluble drugs significantly increased using NDDS. For instance, Curcumin's solubility improved by 35 times when formulated in the NDDS.

Table 2: Particle Size Analysis of NDDS

Formulation Type	Particle Size (nm)	Polydispersity Index (PDI)	Zeta Potential (mV)
Nanoemulsion	150	0.2	-25
Nanocrystals	90	0.1	-30
Liposomes	180	0.3	-20

Nanoemulsions and nanocrystals demonstrated the smallest particle sizes and low PDI, indicating uniform particle distribution. The zeta potential values suggest stable formulations.

Table 3: Drug Release Profile (% Cumulative Release)

Time (Hours)	Pure Drug (%)	NDDS A (Nanocrystals) (%)	NDDS B (Liposomes) (%)
0	0	0	0
2	10	35	25
6	25	70	60
12	40	90	85
24	50	95	90

NDDS significantly enhanced drug release compared to the pure drug. Nanocrystals exhibited the highest cumulative release (95% at 24 hours), indicating improved dissolution properties.

Table 4: Pharmacokinetic Parameters

Parameter	Pure Drug	NDDS A (Nanocrystals)	NDDS B (Liposomes)
Cmax (ng/mL)	100	300	250
Tmax (hours)	6	4	5
AUC (ng·h/mL)	500	1500	1300
Bioavailability (%)	10	30	26

The NDDS formulations significantly improved the bioavailability of the poorly soluble drugs, with nanocrystals achieving the highest Cmax, AUC, and bioavailability.

Table 5: Stability Data (Accelerated Conditions: 40°C, 75% RH)

Parameter	Initial Value	After 1 Month	After 3 Months	After 6 Months
Drug Content (%)	100	98	95	93
Particle Size (nm)	150	155	160	170
Zeta Potential (mV)	-25	-24	-23	-22

The NDDS formulations maintained good stability over six months, with minimal changes in drug content and particle size under accelerated conditions.

Table 6: Cost per Dosage

Formulation Type	Production Cost per Unit ($)	Bioavailability (%)	Cost Effectiveness (Bioavailability/$)
Pure Drug	0.50	10	20
NDDS A (Nanocrystals)	1.00	30	30
NDDS B (Liposomes)	1.20	26	21.7

Although NDDS formulations have higher production costs, the improved bioavailability justifies the investment, particularly for nanocrystals with the highest cost-effectiveness ratio.

Table 7: Toxicity Study Results (Animal Model)

Dose (mg/kg)	Pure Drug (Mortality)	NDDS A (Nanocrystals)	NDDS B (Liposomes)
50	10%	0%	0%
100	20%	5%	5%
200	50%	10%	15%

NDDS formulations showed lower toxicity compared to the pure drug, with nanocrystals exhibiting the least adverse effects, demonstrating their safety for higher doses**.**

CONCLUSION

The development of novel drug delivery systems (NDDS) has proven to be a transformative approach for addressing the challenges associated with poorly soluble drugs. The study systematically demonstrated the effectiveness of NDDS, such as nanocrystals, nanoemulsions, and liposomes, in enhancing the solubility, bioavailability, and therapeutic potential of model drugs like Curcumin, Itraconazole, and Nifedipine. The results showed a significant improvement in solubility, with up to 35-fold enhancement in some formulations, and superior drug release profiles compared to the pure drug. Pharmacokinetic studies confirmed that NDDS formulations could increase the bioavailability of poorly soluble drugs by up to three times, as evidenced by higher Cmax and AUC values. Among the formulations, nanocrystals emerged as the most effective, offering the highest bioavailability enhancement while maintaining stability and safety. NDDS represent a promising solution for improving the therapeutic efficacy of poorly soluble drugs. This study highlights the potential of these advanced systems to overcome solubility and bioavailability barriers, thereby contributing to better patient outcomes and expanding the range of drugs that can be effectively used in clinical practice. Future work should focus on clinical trials to validate these findings and explore their scalability for commercial production.

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