CHALLENGES DUE TO PHARMACEUTICAL DOSAGE FORM DESIGN AND ITS EFFECTS ON PATIENT CHOICES AND COMPLIANCE

BY

EXCEL EFOSA AIGBOSURIA

PHA1706993

FACULTY OF PHARMACY,

UNIVERSITY OF BENIN,

BENIN CITY.

APRIL, 2024

DISSERTATION

A PROJECT SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE AWARD OF DOCTOR OF PHARMACY (PHARM. D) DEGREE.

PRESENTED BY

EXCEL EFOSA AIGBOSURIA

PHA1706993

SUPERVISED BY

PROF MATTHEW I. ARHEWOH

DEPARTMENT OF PHARMACEUTICS AND PHARMACEUTICAL TECHNOLOGY,
FACULTY OF PHARMACY,
UNIVERSITY OF BENIN,
BENIN CITY, NIGERIA.

APRIL, 2024

CERTIFICATION

I certify that this work was carried out by me, **EXCEL EFOSA AIGBOSURIA** a 600-level student of the Faculty of Pharmacy, University of Benin, Benin City.

_____ _____

EXCEL EFOSA AIGBOSURIA **Date**
Project Student

_____ _____

PROF MATTHEW I. ARHEWOH **Date**
Supervisor

_____ _____

PROF. FLORENCE E. EICHIE **Date**
Head of Department

_____ _____

External Examiner **Date**

DEDICATION

I dedicate this project work to God Almighty for his Grace**,** guidance and protection throughout my journey in pharmacy school. And to my parents, Mr. and Mrs. Braimoh O. Aigbosuria for their unending love, support and encouragement.

ACKNOWLEDGMENT

I would like to express my heartfelt gratitude to the Almighty for guiding me throughout this pharmacy school journey, this project and granting me the strength to persevere through its challenges.

To my beloved parents, Mr & Mrs Braimoh O. Aigbosuria whose unwavering support, encouragement, and sacrifices have been the cornerstone of my journey, I owe a debt of gratitude that words cannot fully convey.

To my siblings, Divine, Osas and Osaze, my cousins, Fechi, Arinze, Ebuka your love, understanding, and occasional teasing have brought joy and laughter to my life, making every step of this endeavor more meaningful.

To my dear friends, Prince, Maro, Jennifer, Isi, Edafe Marvellous, thank you for being my pillars of support, for your words of wisdom, and for always believing in me, even when I doubted myself.

This project would not have been possible without the collective love, guidance, and encouragement of these cherished individuals. I am truly blessed to have such an incredible support system in my life.

ABSTRACT

Purpose: The study was carried out to evaluate public knowledge and dosage form preferences among adult participants, assess patient's choices of dosage forms in drug therapy and demonstrate the association of the respondent demographic variables and dosage form preference.

Methods: This study focused on the general population. A pre-tested standardized questionnaire was converted to Google form and distributed to various social media platforms including Instagram, X, WhatsApp and Facebook in March, 2024. Participants were encouraged to provide answers to the questions until over 500 responses were recorded. Responses were evaluated for demographics, knowledge and choices associated with their use of drug dosage forms.

Results: The analysis of the association between demographic variables and patients' dosage form preferences showed that participants exhibited varying preferences with statistically significant associations ($p < 0.05$) for specific dosage forms. Educational status, religion, and occupation demonstrated no significant association ($p > 0.05$) with dosage form preferences, suggesting that patients' educational backgrounds, religion, and occupation may not be decisive factors in determining their preferences. Participants' income however demonstrated a statistically significant association ($p = 0.020$) with dosage form preferences, suggesting that individuals with different income levels may have distinct preferences for specific dosage forms. Overall, these findings underscore the complexity of factors influencing dosage form preferences and emphasize the importance of personalized approaches in medication formulations to cater to the diverse needs of patient populations.

Conclusion: Considering diverse demographic factors and individual preferences in formulating medications influences patients choices and compliance.

TABLE Of CONTENTS

CHAPTER ONE

1.0 INTRODUCTION

Throughout human history, substances derived from plants and minerals, commonly known as drugs, have been in existence. The exploration of these substances has been driven by the necessity to address human diseases and the innate instinct to survive. The utilization of drugs, even in their primitive forms, commenced long before recorded history. It is conceivable that early humans, prompted by the instinct to alleviate pain from wounds, engaged in practices such as bathing wounds in cool water, soothing them with fresh leaves, or protecting them with mud. The empirical knowledge gained from such experiences allowed early humans to discern the effectiveness of certain therapies over others, laying the foundation for the inception of drug therapy (Allen *et al*., 2013).

Medications are seldom administered in their pure chemical form and are typically dispensed as formulated preparations or medicines. These formulations range from uncomplicated solutions to intricate drug delivery systems achieved through the incorporation of suitable additives or excipients. These excipients serve diverse and specialized pharmaceutical purposes. Among other functions, the formulation additives play a crucial role in solubilizing, suspending, thickening, preserving, emulsifying, modifying dissolution, enhancing compatibility, and imparting flavor to drug substances. These processes result in the creation of various medicines or dosage forms (Aulton *et al*., 2013).

Various strategies in drug delivery can be employed to enhance therapeutic effectiveness and minimize side effects by influencing the absorption, distribution, metabolism, and elimination (ADME) of a drug compound. In the case of drugs exhibiting poor water solubility or low permeability, approaches such as amorphous solid dispersion, liposomes, and complexations have proven effective in enhancing their oral bioavailability. Modified release (MR) formulations are widely adopted to enhance patient compliance and mitigate side effects, particularly for drugs with short half-lives or narrow therapeutic windows. While each drug delivery approach has its merits, it also comes with its own set of limitations. Ensuring consistent quality and therapeutic performance using drug delivery

systems presents significant challenges in the development of drugs for both brand and generic versions. Achieving this consistency demands close collaboration among industry, academia, and regulatory agencies, emphasizing the need for a comprehensive and cooperative approach (Wen *et al*., 2015).

Ensuring appropriate dosage forms is crucial for successful pharmacotherapy. Creative dosage forms or delivery systems have the potential to target a drug precisely to its intended site of action, refine the timing of drug release, or enhance patient comfort and convenience. Consequently, these innovations can contribute to enhanced efficacy and tolerability, ultimately resulting in improvements in the overall health-related quality of life (Frijlink, 2003).

Patients assume a crucial role in attaining the intended therapeutic results, given their frequent responsibility for managing their medications. To enhance drug administration and address medication-related challenges, it is imperative to take into account the patients' needs and preferences during the design of pharmaceutical drug products (Drumond *et al*., 2017). There is a growing body of evidence indicating that anticipated clinical outcomes in real-world treatment scenarios often fall short. Recent analyses of the observed disparities between efficacy and effectiveness suggest that factors such as patient perception, therapy management, health literacy, adverse reactions, and challenges in navigating healthcare systems significantly contribute to these gaps (Eichler *et al*., 2011).

1.1 History and Evolution of Dosage Form Development

The historical development of dosage formulations traces back to the evolution of drug discovery and development throughout human history. Dating back to ancient civilizations, drugs served not only as physical remedies but were also associated with religious and spiritual healing. In those times, sages or religious leaders often administered drugs, primarily derived from plant products and supplemented by animal materials and minerals. The discovery of these early drugs was likely a result of trial-and-error experimentation, coupled with the observation of human and animal reactions to ingesting such products (Helfand *et al*., 1983).

The transition to a more scientific approach in drug discovery and development occurred in the late 1800s, marking the departure from the extraction of drugs from natural sources in small batches to large-scale manufacturing plants. Following World War I, the modern pharmaceutical industry emerged, firmly establishing drug discovery and development on scientific principles. The historical narrative of dosage formulations unfolds as a captivating journey through time, encapsulating the progression of pharmaceutical science into tangible medicinal forms (Helfand *et al*., 1983; Mahato *et al*., 2017).

In ancient civilizations such as Egypt, Mesopotamia, China, and India, the early approaches to drug administration were deeply intertwined with nature. Herbal remedies, including teas, infusions, and poultices, took center stage as primary dosage forms for treating ailments. The Middle Ages witnessed a more structured approach to drug preparation, with apothecaries and pharmacists recognizing the importance of standardization and compounding medicines based on physicians' prescriptions (Helfand *et al*., 1983).

The Renaissance period saw the emergence of more defined dosage forms, including pills, powders, and tinctures. The 17th century marked a significant milestone with the introduction of pharmacopoeias, formalizing drug formulations and dosages. Technological advancements in the 19th century revolutionized pharmaceutical manufacturing, enabling mass production of standardized dosage forms with the introduction of tablet presses, coating machines, and improved processes. Gelatin capsules in the early 20th century provided a tasteless and convenient alternative for accommodating both liquid and dry formulations (Jackson *et al*., 2005; Mahato *et al*., 2017).

The mid-20th century witnessed further progress in formulation science with the development of controlled-release and sustained-release formulations, altering the landscape of drug administration. The late 20th century brought forth advanced drug delivery systems, including transdermal patches and inhalers, aimed at enhancing drug efficacy and patient compliance. The 21st century is characterized by the integration of cutting-edge technologies into drug formulation, such as nanotechnology and biotechnology, enabling targeted drug delivery for improved bioavailability and reduced side effects (Alvarez-Lorenzo *et al*., 2013).

The overarching historical trajectory of dosage formulations reflects the persistent pursuit of excellence in pharmaceutical science. From ancient herbal concoctions to the sophisticated personalized medicine of today, each era has contributed to the refinement of drug administration and formulations. This historical journey underscores the commitment of scientists, pharmacists, and researchers to continually enhance the safety, efficacy, and overall patient experience in the realm of pharmaceuticals (Helfand *et al*., 1983; Alvarez-Lorenzo *et al*., 2013).

1.2 Drug Delivery, Principles of Dosage Form Design and Routes of Drug Administrations

In the 1980s and 1990s, innovative drug delivery systems were successfully introduced, primarily through the development of sustained-release (controlled-release) oral formulations or transdermal patches. These novel dosage forms found applications predominantly in therapeutic areas like hypertension, angina, arthritis, smoking cessation, and hormone replacement therapy—specifically targeting chronic diseases or conditions demanding prolonged (potentially lifelong) drug therapy (Seager, 1998). An added advantage of advanced controlled-release formulations, exemplified by drugs such as verapamil, nifedipine, metoprolol, nitroglycerine, morphine, fentanyl, and estrogens, is the increased economic value attributed to simplified administration regimens (enhancing compliance) and regulated drug input, preventing plasma drug concentrations from reaching super- or subtherapeutic levels (Cramer and Saks, 1994).

The primary goal in designing dosage forms is to achieve a consistent therapeutic response to a drug incorporated in a formulation that is suitable for large-scale production with consistently reproducible product quality. Ensuring product quality involves multiple aspects, including chemical and physical stability, adequate protection against microbial contamination if applicable, uniform drug dosing, acceptability to both prescribers and patients, and appropriate packaging and labeling. Ideally, dosage forms should also minimize variation among individual patients, although achieving this remains challenging in practice. However, recent advancements are starting to address this need, incorporating features such as drug delivery systems responsive to the specific metabolic activity of

individual patients and implants triggered by external stimuli like sound or magnetic fields (Aulton *et al*., 2013).

A variety of dosage forms are available for the effective treatment of diseases, allowing for administration through different routes to optimize therapeutic outcomes. These preparations can be taken orally, injected, applied to the skin, or inhaled. Nevertheless, it is essential to align the drug substance with the specific clinical indication being treated before determining the appropriate combination of drug and dosage form. Each disease or illness often requires a tailored drug therapy. Additionally, considerations such as the chosen administration route and its specific requirements affecting drug absorption must be factored in when designing dosage forms (Aulton *et al*., 2013).

The way drugs are absorbed shows significant variation not only among individual drug substances but also across various administration routes. Dosage forms are created to offer the drug in a form conducive to absorption from the chosen route of administration. These routes and some their specific advantages and disadvantages encompass:

1. Oral administration, suitable for patients capable of ingesting and tolerating oral medications, often involves timed-release or sustained-release forms for drugs with short half-lives, facilitating absorption over several hours (Jain 2020). Benefits include ease of administration and broad acceptance among patients, yet drawbacks include variable absorption rates and the potential degradation of drugs before reaching the bloodstream due to factors such as low pH levels in the digestive tract and hepatic metabolism (Jain 2020).
2. Sublingual and buccal routes are utilized for drugs with high first-pass metabolism, such as nitroglycerin, offering advantages like rapid absorption and the ability to remove the tablet if needed, while drawbacks include challenges in tablet placement and potential palatability issues (Jain 2020).
3. Rectal administration is beneficial for patients with gastrointestinal motility problems or those in hospice care, providing advantages like the ability to administer large drug quantities and bypass hepatic metabolism, but limitations include potential rectal irritation and the unsuitability of certain drugs for rectal absorption (Levy *et al*., 1990).

4. Intravenous administration delivers drugs directly to the systemic circulation, offering rapid onset and predictable bioavailability, yet drawbacks include pain and the risk of infection (Jain 2020).
5. Intramuscular administration may be preferred for drugs with erratic oral absorption or high first-pass metabolism, but drawbacks include injection site pain and the risk of complications such as hematoma or abscess (Gutierrez *et al*., 2023).
6. Subcutaneous administration is employed for drugs with poor oral absorption or when faster absorption is required, with benefits like ease of administration and minimal skill requirements, but limitations include difficulties in controlling absorption rates and the need to change injection sites frequently to prevent tissue injury (Jain 2020).
7. Intranasal administration is used for nasal decongestants and other drugs, offering advantages like increased permeability and rapid absorption, yet limitations include the potential impact of nasal cavity diseases on drug absorption (Jain 2020).
8. Inhalational administration allows for efficient drug absorption due to the large surface area of the alveolar epithelium, but challenges include overcoming aerodynamic filters and mucus clearance (Jain 2020).
9. The vaginal route permits low, continuous dosing of medications and is utilized for various formulations, including tablets and creams, but is less commonly used compared to other routes (Srikrishna *et al*., 2013).
10. Transdermal administration, facilitated by techniques like iontophoresis and microneedles, offers controlled drug delivery through the skin, representing an evolving area in drug delivery systems (Jain 2020).

1.3 Dosage Formulations: Definition and Types

Pharmaceutical formulation is a complex process involving multiple steps, where the active drug is combined with various components, taking into account factors such as particle size, polymorphism, pH, and solubility, to produce the final medicinal product with therapeutic benefits. The key elements for successful pharmaceutical formulation include the active pharmaceutical ingredients (APIs), essential excipients, their interactions, and the manufacturing process. The formulation typically serves different functions and takes the

form of various dosage forms, representing the pharmaceutical drug product available for use with a specific combination of active and inactive components. It must have a specific configuration, such as a capsule shell, and be distributed in a particular dose (Afrin *et al*., 2020).

Pharmaceutical formulation encompasses the creation of a pharmaceutical product, encompassing the chemical properties of the drug, its formulation, and details of the treatment protocol intended for clinical application (Stewart *et al*., 2016). Currently, there are tens of thousands of medication formulations accessible for clinicians to prescribe and for patients to use (Seddon *et al*., 2012; Snell *et al*., 1985).

Dosage forms, also known as unit doses, are pharmaceutical drug products designed for use in a specific form, comprising a distinct combination of active ingredients and inactive components (excipients), arranged in a particular configuration, such as a capsule shell, and measured into a specific dose (Ahmed *et al*., 2016). Each category of dosage form possesses unique physical and pharmaceutical characteristics. The diverse preparations pose formulation challenges for manufacturing and compounding pharmacists, while offering physicians choices in selecting both the drug and the delivery system to prescribe. The broader field of study addressing the formulation, production, stability, and efficacy of pharmaceutical dosage forms is referred to as pharmaceutics (Allen *et al*., 2013).

The effective design and creation of a dosage form necessitate a thorough assessment of the physical, chemical, and biological attributes of all drug substances and pharmaceutical ingredients intended for use in manufacturing the product. To ensure stability, effectiveness, visual appeal, ease of administration, and safety, there must be compatibility between the drug and pharmaceutical materials utilized in producing the drug product (Allen *et al*., 2013).

Apart from facilitating the secure and convenient delivery of precise doses, dosage forms serve additional purposes:

1. Safeguarding the drug substance from detrimental effects of atmospheric oxygen or humidity (e.g., coated tablets, sealed ampuls).
2. Shielding the drug substance from the corrosive impact of gastric acid following oral administration (e.g., enteric-coated tablets).

3. Concealing the bitter, salty, or unpleasant taste or odor of a drug substance (e.g., capsules, coated tablets, flavored syrups).
4. Offering liquid preparations of drug substances, either as dispersions (suspensions) or clear solutions.
5. Enabling rate-controlled drug action through various controlled-release tablets, capsules, and suspensions.
6. Ensuring optimal drug action from topical administration sites (e.g., ointments, creams, transdermal patches, and ophthalmic, ear, and nasal preparations).
7. Facilitating drug insertion into body orifices (e.g., rectal or vaginal suppositories).
8. Facilitating the placement of drugs directly into the bloodstream or body tissues through injections.
9. Enabling optimal drug action through inhalation therapy (e.g., inhalants and inhalation aerosols).

(Allen *et al*., 2013).

The various types of dosage formulations available for pharmaceutical preparations include:

1.3.1 Tablets

Tablets represent the predominant dosage form, with approximately 70% of all medications being distributed in this format. The characteristics of tablets, including their shapes, sizes, and weight, vary based on the medicinal substances they contain and the intended method of administration (Ubhe *et al*., 2020).

As per the Indian Pharmacopoeia, pharmaceutical tablets are compact, flat, or biconvex dishes, constituting a unit dosage form. These tablets are created by compressing drugs or a combination of drugs, with or without diluents. A tablet is specifically described as a compressed solid form containing medicinal substances, with or without additional excipients. The shapes, sizes, and weights of tablets vary significantly, contingent on the quantity of medicinal substances involved and the intended method of administration (Lachman *et al*., 1976; Ubhe *et al*., 2020).

Properties of an ideal tablets include:

i. The product should possess an attractive appearance, establishing its unique identity while remaining devoid of imperfections such as chips, cracks, discoloration, and contamination.
ii. It should exhibit the necessary strength to endure the challenges posed during its production, packaging, shipping, and dispensing, effectively withstanding various shocks.
iii. The product must demonstrate physical stability, preserving its inherent attributes consistently over an extended period.
iv. It is imperative for the product to release the medicinal agent(s) in the body in a manner that is both predictable and reproducible.
v. The product must maintain suitable chemical stability over time to prevent any alteration of the medicinal agent(s).

(Ubhe *et al*., 2020)

Advantages of tablets include their status as a unit dosage form, offering superior capabilities for precise dosing and minimal content variability. They are recognized for their cost-effectiveness, ease of packaging and stripping, light and compact nature, excellent chemical and microbial stability among all oral dosage forms, and suitability for large-scale production. Tablets are easy to swallow with minimal hang-up, and any objectionable odor or bitter taste can be effectively masked using coating techniques. Additionally, sustained release products are achievable through enteric coating, and tablets are convenient to handle (Ubhe *et al*., 2020: Allen *et al*., 2013).

However, there are notable disadvantages. Tablets can pose difficulties for swallowing, particularly for children and unconscious patients. Some drugs, due to their amorphous nature and low density, resist compression into dense compacts. Drugs with poor wetting, slow dissolution properties, and optimal absorption high in the gastrointestinal tract may be challenging to formulate or manufacture as tablets while ensuring adequate drug bioavailability. Bitter-tasting drugs, those with objectionable odors, or those sensitive to oxygen may require encapsulation or coating, with capsules potentially offering a more cost-effective solution. Furthermore, tablets may cause irritant effects on the gastrointestinal

mucosa, such as with aspirin, and there is a possibility of bioavailability problems arising from slow disintegration and dissolution (Ubhe *et al*., 2020: Allen *et al*., 2013).

Excipients used in tablet formulation encompass diluents, which act as fillers to increase tablet bulk when the drug dosage alone is insufficient, enhancing cohesion and facilitating direct compression. Binders are employed to create cohesive compacts for directly compressed tablets. Lubricants serve to prevent adhesion of tablet materials to dies and punches, reduce inter-particle friction, and potentially improve the flow rate of tablet granulation. Glidants are designed to promote the flow of granules or powder material by reducing friction between particles. Anti-adherents are added to tablet formulations to prevent material adherence to the walls of the tablet press (Ubhe *et al*., 2020: Allen *et al*., 2013).

Disintegrates are included in tablet formulations to facilitate breaking or disintegration upon contact with water in the gastrointestinal tract. Coloring agents serve three purposes: masking off-color drugs, product identification, and enhancing the tablet's aesthetic appeal. Flavoring agents, crucial for chewable tablets, are typically added in dry forms such as spray-dried beadlets. Absorbents are necessary in tablet formulations containing substances with a high affinity to water, as hygroscopic materials can render the blend wet and challenging to handle during manufacture (Ubhe *et al*., 2020: Allen *et al*., 2013).

1.3.1.1 Types of Tablets

Some tablet types available in pharmaceutical preparations include:

i. **Enteric-coated tablets**: These tablets are coated with a special layer that prevents dissolution in the stomach while ensuring dissolution in the intestine. This coating serves to protect the medication from degradation by gastric juice in the stomach, facilitating absorption in the intestine. Additionally, the coating enhances absorption and minimizes irritation to the stomach lining (Hussan *et al*., 2012).

ii. **Sublingual tablets**: Specifically designed to be placed beneath the tongue, sublingual tablets enable direct absorption into the bloodstream through the mucosal membrane. This administration method leads to faster therapeutic effects compared to oral administration. An example includes trinitrate tablets (Jaiswani *et al*., 2014).

iii. **Effervescent tablets**: This type of oral pharmaceutical formulation rapidly dissolves in water, creating a fizzy or effervescent solution. Typically containing an active ingredient (such as medication or vitamins) along with effervescent agents like sodium bicarbonate and citric acid, these tablets induce a chemical reaction that releases carbon dioxide gas when dissolved in water. Effervescent tablets offer ease of administration and increased bioavailability (Patel *et al*., 2018).

iv. **Chewable tablets**: Meant to be chewed, these tablets break down into smaller pieces, increasing the surface area exposed for the dissolution process. This design allows for quicker absorption of released medicines in the body. Chewable tablets are often administered to individuals facing difficulty swallowing, such as the elderly and children, or when the prescribed dose is too large (Renu *et al*., 2015).

1.3.2 Capsules

Medicinal substances or inert components are enclosed within a small gelatin shell known as a capsule, which can be either hard or soft based on its composition. These capsules may consist of two parts, a body and a cap, or be a single-piece structure. Two-piece capsules are commonly known as hard-shell capsules, while one-piece capsules are referred to as soft-shell capsules. The standard use for filled capsules is to be swallowed whole; however, in certain healthcare settings, caregivers might open capsules or crush tablets for patients unable to swallow solid forms. This practice requires pharmacist approval, as altering the drug-release characteristics can impact patient well-being (Allen *et al*., 2013).

i. **Hard Gelatin Capsules**: Hard gelatin capsule shells are prevalent in commercial medicated capsules, clinical drug trials, and community pharmacy compounding. These capsules, composed of gelatin, sugar, and water, can be transparent, colorless, and nearly tasteless. Coloring agents and opaquing agents like titanium dioxide are often added, resulting in distinctive appearances, often with differently colored caps and bodies. Gelatin is derived from collagen found in animal skin, connective tissue, and bones. In various forms like fine powder, coarse powder, shreds, flakes, or sheets, gelatin is commercially available (Kathpalia *et al*., 2014).

ii. **Soft Gelatin Capsules**: Soft gelatin capsules, made by adding glycerin or a polyhydric alcohol like sorbitol to gelatin, may include preservatives such as methylparaben or propylparaben to inhibit microbial growth due to their higher moisture content. These capsules can be oblong, oval, or round, single-colored or two-toned, and may feature identifying imprints. Similar to hard gelatin capsules, they can be formulated with opaquants for reduced transparency and distinctive capsule characteristics. Soft gelatin capsules are well-suited for encapsulating liquids, suspensions, pasty materials, dry powders, and preformed tablets, presenting a pharmaceutically elegant solution that is easily swallowed (Gullapalli 2010).

1.3.3 Ointments, Creams and Gels (Semi-Solid Preparations)

Ointments, creams, and gels are semisolid forms of medication designed for topical application, whether on the skin, the surface of the eye, or in areas like the nose, vagina, or rectum. While most of these formulations are utilized for the therapeutic effects of the medicinal agents they contain, unmedicated ones serve as protectants or lubricants (Garg *et al*., 2014; Allen *et al*., 2013).

These topical preparations serve both local and systemic purposes. It's crucial to consider systemic drug absorption, especially in pregnant or nursing patients, as drugs can potentially enter the fetal bloodstream or breast milk. Ointments, semisolid preparations for external application to the skin or mucous membranes, may be medicated or unmedicated. Unmedicated ointments are employed for their physical effects, functioning as protectants, emollients, or lubricants (Allen *et al*., 2013; Maqbool *et al*., 2017).

Pharmaceutical creams are semisolid formulations with medicinal agents dissolved or dispersed in water-in-oil (W/O) emulsions, oil-in-water (O/W) emulsions, or another water-washable base. Vanishing creams, for instance, are oil-in-water emulsions with significant water content. Creams are widely used in skincare and mucous membrane products, offering advantages such as easier spreadability and removal compared to ointments. Manufacturers often produce drug formulations in both cream and ointment bases to accommodate patient and physician preferences (Chauhan *et al*., 2020; Allen *et al*., 2013).

Creams, with a soft and spreadable consistency, can be further categorized as non-washable or washable based on their emulsion type. Gels, or jellies, are semisolid systems containing dispersed small or large molecules in an aqueous liquid vehicle, imparting a jelly-like consistency through the addition of gelling agents such as synthetic macromolecules (e.g., carbomer 934), cellulose derivatives (e.g., carboxymethylcellulose or hydroxypropyl methylcellulose), or natural gums (e.g., tragacanth). Carbomers, specifically, are high molecular weight water-soluble polymers of acrylic acid cross-linked with allyl ethers of sucrose and/or pentaerythritol, with viscosity depending on their polymeric composition (Allen *et al*., 2013).

Other miscellaneous semi-solid dosage formulations include pastes, plasters, glycogelatin and others (Allen *et al*., 2013).

1.3.4 Suppositories

A suppository represents a solid form of medication where one or more active pharmaceutical ingredients (APIs) are dispersed in a suitable base, taking on a shape suitable for insertion into the rectum to induce local or systemic effects. These solid dosage forms are designed for insertion into body orifices, where they undergo melting, softening, or dissolution, thereby exerting either local or systemic effects. The term "suppository" is derived from the Latin word "supponere," meaning "to place under," combining "sub" (under) and "ponere" (to place). Consequently, suppositories are linguistically and therapeutically intended to be positioned beneath the body, such as into the rectum (Allen *et al*., 2013).

On the other hand, an insert is a solid dosage form that is placed into a naturally occurring (non-surgical) body cavity other than the mouth or rectum, encompassing locations like the vagina and urethra. Medication sticks serve as a convenient form for administering topical drugs, and their development is intriguing as it intertwines with the historical evolution of cosmetics, reflecting the parallel trajectory of human history (Allen *et al*., 2013).

1.3.5 Transdermal Patches

A transdermal patch serves as a means to administer a specific dosage of medication through the skin and into the bloodstream. FDA approval for transdermal patch products was initially granted in 1981. Presently, transdermal delivery systems encompass products containing scopolamine (hyoscine) for motion sickness, clonidine, and nitroglycerin for cardiovascular disease, fentanyl for chronic pain, and nicotine for smoking cessation assistance. This mode of drug delivery ensures controlled and constant administration, offering advantages over conventional injection and oral methods (Gaur *et al*., 2009).

Key benefits of transdermal patches include continuous drug input for substances with short biological half-lives, reduced digestive tract and liver load compared to oral routes, enhanced patient compliance, and minimized side effects from temporary overdose. The convenience is particularly notable in patches requiring only weekly application, facilitating patient adherence to drug therapy (Gaur *et al*., 2009).

The primary components of a transdermal patch include:

i. **Polymer Matrix**: Serves as the backbone, controlling drug release. The polymer should be chemically non-reactive, non-toxic, and cost-effective. Examples include cellulose derivatives, zein, gelatin, waxes, gums, and various synthetic polymers.
ii. **Drug**: The transdermal route is advantageous for drugs with suitable pharmacology and physical chemistry, especially those undergoing extensive first-pass metabolism, having a narrow therapeutic window, or a short half-life (e.g., fentanyl, nitroglycerin).
iii. **Permeation Enhancers**: Increase stratum corneum permeability to achieve higher therapeutic drug levels. They include lipophilic solvents, surface-active agents, and two-component systems (e.g., DMSO).
iv. **Adhesive**: Facilitates higher therapeutic drug levels by increasing stratum corneum permeability.
v. **Backing Laminates**: Should possess low modulus or high flexibility (e.g., vinyl, polyethylene).
vi. **Release Liner**: Protects the patch during storage and is removed before use.
vii. **Other Excipients**: Such as plasticizers and solvents (Aggarwal *et al*., 2009).

1.3.6 Inhalers (Dry Powder Inhalers)

Dry powder inhalers (DPIs) function as devices delivering a dry powder formulation of an active drug through the pulmonary route for either local or systemic effects (Peart *et al*., 2001). Inhalation drug delivery systems fall into three main categories: pressurized metered dose inhalers, dry powder inhalers, and nebulizers, each with distinct strengths and weaknesses. Among these, dry powder inhalers play a pivotal role by facilitating the pulmonary delivery of higher doses, particularly for locally acting drugs like sodium cromoglycate. They also serve as an alternative for patients who struggle with coordinating the discharge and inhalation of pressurized metered dose inhalers (MDIs). Dry powder inhalers, categorized as bolus drug delivery devices, contain solid drugs either suspended or dissolved in a non-polar volatile propellant or in a dry powder that fluidizes upon patient inhalation (Dolovich *et al*., 2005; Barry *et al*., 2003).

Dry powder inhalers offer several advantages over other pulmonary drug delivery methods, such as direct drug delivery into the deep lungs, utilizing the patient's respiration. They are increasingly explored as a mechanism for delivering systemic drugs. Successful drug delivery into the deep lung relies on the integration of powder formulations and device performance. Current DPIs seeking licensing and marketing approval must demonstrate both in vitro performance and in vivo efficacy and reliability (Alagusundaram *et al*., 2010).

i. An ideal dry powder inhaler should possess the following key characteristics:
ii. Ensure effective dosing with a uniform dose throughout the device's lifespan.
iii. Provide targeted and optimized delivery, maintaining a controlled respirable fraction.
iv. Allow inhalation of dose-independent aerosol generation.
v. Offer a bolus of aerosol at the beginning of an inhalation.
vi. Be operable at low inhalation flow rates.
vii. Exhibit efficiency in terms of environmentally friendly production.
viii. Undergo design optimization through practical engineering and manufacturing innovation.
ix. Incorporate in-process controls to ensure quality.
x. Maintain a compact, portable, inexpensive, and reusable design.
xi. Provide clear comparative data for addressing complaints.

xii. Be user-friendly, featuring a simple operation, dose counter, dose-ready indicator, and mechanisms for patient feedback on dose administration (Alagusundaram *et al*., 2010).

1.3.7 Parenteral Dosage Forms (Injections)

Injections are preparations that are sterile and free from pyrogens (limited to endotoxin units [EU]), designed for parenteral administration. The term "parenteral" refers to routes of administration involving injection, originating from the Greek words "para" (outside) and "enteron" (intestine), indicating routes other than oral administration. Pyrogens, or bacterial endotoxins, are organic products released by gram-negative bacteria, potentially causing fever and hypotension in excessive amounts in intravenous (IV) injections. The presence of pyrogens in parenteral preparations is discussed later in this chapter. Generally, parenteral routes are chosen for situations requiring rapid drug action, emergencies, uncooperative or unconscious patients, or when oral medication acceptance or tolerance is not possible. Except for self-administered insulin injections, typically done by diabetics, healthcare professionals like physicians, physician's assistants, or nurses administer most injections during medical treatments. Injections are primarily utilized in hospital settings, extended care facilities, clinics, and occasionally at home, notably in home health care programs where professionals visit patients to provide necessary treatment, including IV medications. These programs enable patients who don't need expensive hospitalization or can't afford it to receive medical care at home. Pharmacists supply injectable preparations to healthcare providers for use in institutional settings, clinics, offices, or home health care programs (Allen *et al*., 2013).

The earliest officially recognized injectable drug was hypodermic morphine solution, introduced in the 1874 addendum to the 1867 British Pharmacopeia and the 1888 edition of the National Formulary (NF) of the United States. Today, a vast array of drugs and drug products are available for parenteral administration. Drugs can be injected into various body organs or areas, including joints (intraarticular), joint fluid areas (intrasynovial), spinal column (intraspinal), spinal fluid (intrathecal), arteries (intra-arterial), and even the heart (intracardiac) in emergencies. However, the majority of injections are administered into

veins (intravenous, IV), muscles (intramuscular, IM), skin (intradermal, ID; intracutaneous), or under the skin (subcutaneous, SC; sub-Q, SQ; hypodermic, hypo) (Allen *et al*., 2013).

1.3.8 Liquid Dosage Forms (Solutions, Syrups, Tinctures, Elixirs)

Pharmaceutical solutions encompass liquid formulations containing one or more chemical substances dissolved in a suitable solvent or a blend of mutually miscible solvents, as defined by the USP 2012 (United States Pharmacopeia, 2012). These solutions are classified based on their pharmaceutical use, such as oral, otic, ophthalmic, or topical, and can also fall into other dosage form categories. For example, aqueous solutions with sugar are designated as syrups (although some may contain alcohol), sweetened hydroalcoholic solutions are termed elixirs, and solutions of aromatic materials are referred to as spirits if the solvent is alcoholic or aromatic waters if the solvent is aqueous. Solutions prepared by extracting active constituents from crude drugs are termed tinctures or fluidextracts, and tinctures may also denote solutions of chemical substances dissolved in alcohol or hydroalcoholic solvents. Sterile and pyrogen-free solutions intended for parenteral administration are categorized as injections (Allen *et al*., 2013).

Oral solutions, syrups, elixirs, spirits, and tinctures serve distinct purposes, delivering medicinal agents for systemic effects (American Society of Hospital Pharmacists, 1987; Pesko, 1983). Being soluble in aqueous systems, orally administered solutions typically facilitate faster absorption from the gastrointestinal tract into the systemic circulation compared to suspension or solid dosage forms of the same medicinal agent. These solutions often contain solutes other than the medicinal agent, such as colorants, flavorings, sweeteners, or stabilizers. In formulating pharmaceutical solutions, pharmacists must consider the solubility and stability of each solute in relation to the solvent or solvent system to avoid interactions that could affect the therapeutic quality or pharmaceutical stability (Allen *et al*., 2013).

Liquid pharmaceuticals for oral administration are formulated to provide the patient with the standard dose of medication in convenient volumes, such as teaspoons or tablespoons. Syrups, concentrated aqueous preparations of sugar with or without flavoring agents and medicinal substances, can be medicated or nonmedicated. Nonmedicated syrups, also known

as flavored vehicles, serve as pleasant-tasting bases for medicinal substances added in extemporaneous compounding or the preparation of medicated syrups containing therapeutic agents. Due to challenges faced by certain populations, like children and the elderly, in swallowing solid dosage forms, pharmacists are frequently requested to prepare oral liquid dosage forms. The choice between a solution or a suspension depends on the chemical and physical characteristics of the specific drug and its solid dosage form, with commercially available vehicles designed for compounding purposes. Elixirs, clear, sweetened hydroalcoholic solutions intended for oral use, are flavored for enhanced palatability. Nonmedicated elixirs function as vehicles, while medicated elixirs provide therapeutic effects (Allen *et al*., 2013).

Tinctures, alcoholic or hydroalcoholic solutions, are prepared from vegetable materials or chemical substances, varying in preparation method, active ingredient strength, alcoholic content, and intended use in medicine or pharmacy. When derived from chemical substances (e.g., iodine, thimerosal), tinctures involve a simple solution of the chemical agent in the solvent (Allen *et al*., 2013).

1.3.9 Disperse Systems (Suspensions, Emulsions)

Suspensions are defined as formulations containing finely divided drug particles (the suspensoid) distributed somewhat evenly throughout a vehicle where the drug demonstrates minimal solubility. Some suspensions are readily available, pre-distributed in a liquid vehicle, either with or without stabilizers and other additives. Conversely, other preparations are in the form of dry powders meant to be suspended in liquid vehicles. Typically, these products consist of a powder blend containing the drug and appropriate suspending and dispersing agents, which can be diluted and agitated with a specified amount of vehicle, commonly purified water. Drugs prone to instability over extended periods in the presence of an aqueous vehicle, such as many antibiotics, are frequently provided as dry powder mixtures, to be reconstituted at the time of dispensing. This category of preparation is labeled in the USP with a title like "for Oral Suspension." Suspensions that do not require reconstitution at the time of dispensing are simply designated as "Oral Suspension" (Allen *et al*., 2013).

An emulsion refers to a dispersion in which small globules of a liquid, known as the dispersed phase, are distributed throughout a vehicle in which they are immiscible. Emulsion terminology designates the dispersed phase as the internal phase, and the dispersion medium as the external or continuous phase. Emulsions with an oleaginous internal phase and an aqueous external phase are labeled as oil-in-water (o/w) emulsions. Conversely, emulsions with an aqueous internal phase and an oleaginous external phase are referred to as water-in-oil (w/o) emulsions. Since the external phase of an emulsion is continuous, an o/w emulsion can be diluted or extended with water or an aqueous preparation, while a w/o emulsion can be extended with an oleaginous or oil-miscible liquid (Allen *et al*., 2013).

To achieve stability in emulsions, a third phase, an emulsifying agent, is typically required. The viscosity of emulsions can vary significantly based on their constituents, and pharmaceutical emulsions may be formulated as either liquids or semisolids. Depending on their constituents and intended applications, liquid emulsions can be administered orally, topically, or parenterally, while semisolid emulsions are generally used topically. It's worth noting that many pharmaceutical preparations that technically qualify as emulsions may not be officially classified as such if they more appropriately fit another pharmaceutical category (Allen *et al*., 2013).

1.4 Common Challenges in Dosage Formulation

1.4.1 Stability and Shelf-Life Issues

Ensuring the stability and extending the shelf life of pharmaceutical dosage forms is a critical challenge in formulation (Lucas *et al*., 2004). Various factors, such as chemical degradation, physical changes, and microbial contamination, can compromise the stability of drugs in different formulations. For instance, the presence of reactive functional groups may lead to chemical degradation, and exposure to light, heat, or moisture can accelerate these processes (Waterman *et al*., 2011). Formulation scientists must carefully select excipients and packaging materials that minimize these risks (Lucas *et al*., 2004).

In addition, the interaction between drug substances and excipients, known as incompatibilities, can contribute to stability issues. Excipients, while crucial for formulation, may react with the active pharmaceutical ingredient (API), leading to degradation or altered drug release characteristics (Waterman *et al*., 2011). Thorough compatibility studies are essential during formulation development to mitigate such risks and ensure the stability of the final dosage form (Allen *et al*., 2013).

Furthermore, the pharmaceutical industry faces challenges in predicting and extending the shelf life of formulations. Accelerated stability studies, real-time stability studies, and modeling approaches are employed to estimate shelf life, but uncertainties persist due to the complex nature of drug degradation pathways (Lucas *et al*., 2004). Addressing stability challenges requires a multidisciplinary approach, combining pharmaceutical science, analytical chemistry, and material science (Allen *et al*., 2013).

1.4.2 Palatability and Taste Considerations

Achieving palatability in oral dosage forms, especially for pediatric and geriatric populations, is a significant challenge (Ternik *et al*., 2018). The taste of a pharmaceutical product can significantly impact patient adherence, especially in the case of liquid formulations or orally disintegrating tablets. Unpleasant tastes may lead to non-compliance, particularly in pediatric patients who may resist medication due to aversion to bitter or unpleasant flavors (Ternik *et al*., 2018).

Masking the taste of drugs, particularly those with inherently bitter or unpleasant flavors, often requires innovative formulation approaches. Encapsulation technologies, flavoring agents, and taste-masking excipients are employed to enhance palatability (Ternik *et al*., 2018). Additionally, formulators must consider the stability of taste-masking agents and their potential interaction with the drug substance (Aulton *et al*., 2013).

1.4.3 Complex Dosing Regimens

The development of pharmaceutical formulations with complex dosing regimens poses challenges related to patient adherence and convenience. Patients may struggle to adhere to

treatment plans that involve multiple doses per day, different dosage forms, or specific administration requirements. Complex regimens can impact therapeutic outcomes and decrease patient compliance, particularly in chronic diseases where long-term medication is necessary (Homayun *et al*., 2019).

Simplifying dosing regimens through the development of extended-release formulations, fixed-dose combinations, or innovative drug delivery systems is crucial for enhancing patient adherence (Homayun *et al*., 2019).

1.5 Patient-Centered Dosage Form Design

The amalgamation of patient-centricity and the design of pharmaceutical drug products gives rise to a more precise term, referred to as "patient-centric pharmaceutical drug product design." This concept signifies an approach that aligns the characteristics of a product directly with those of the patient for a therapeutic objective within a specific patient population(s). It necessitates a well-defined description that can be consistently applied among key stakeholders. The definition also underscores the importance of considering human (patient) characteristics in the product design. For instance, a primary package closure system should not only meet its functional requirements of safeguarding the product from environmental contamination and ensuring stability but should also incorporate features like easy opening and reclosing, or facilitating precise dose measurement for caregivers and/or patients with limited manual dexterity, grip strength, or visual capacity (Stegemann *et al*., 2016).

The administration of medication is a fundamental aspect of contemporary medical practice, emphasizing the importance of delivering the correct drug to the right patient, in the right dose, through the appropriate route, and at the designated time (McGillicuddy *et al*., 2017). The concept of "patient centricity" is gaining prominence, both in academic discourse and the pharmaceutical industry, reflecting a growing inclination among pharmaceutical companies to develop products that align with user needs to enhance acceptability. The design of patient-centric medicine is considered instrumental in improving the quality of life for patients (McGillicuddy *et al*., 2017).

Patient-centric medicine design is characterized as a process that identifies and addresses the comprehensive needs of a target population, culminating in a formulation that offers the best overall benefit-to-risk profile (Stegemann *et al*., 2016). Recent recommendations from the European Medicines Agency (EMA) emphasize the importance of considering physical characteristics, such as the size and shape of tablets or capsules, in pharmaceutical design, especially for the older population, a major demographic for prescribed medicines (EMA, 2020).

The term "patient acceptability," defined as "an overall ability of the patient and caregiver to use a medicinal product as intended" (Kozarewicz, 2014), is central to discussions about these characteristics, according to both the EMA and FDA (EMA, 2020). Patient acceptability significantly influences adherence, defined by NICE as "the extent to which the patient's action matches the agreed recommendations." When designing drug products for the elderly, the heterogeneous nature of this population poses challenges. Consideration must be given to co-morbidities and age-related changes in cognition, motor functions, and sensory functions (Wahlich *et al*., 2013). Age-related alterations, such as diminished hand–eye coordination, trembling hands, impaired manual dexterity, and dysphagia, can substantially impact the medication-taking process (EMA, 2020).

The complexities associated with drug therapy for older individuals extend to the increased responsibilities of informal (family) carers in the community, particularly evident in conditions like dementia. Informal carers often find managing medication challenging, further complicating adherence to treatment plans (Aston *et al*., 2017). Various factors associated with drug therapy, such as the number of medications, treatment duration, tablet characteristics, and dosage regimen, contribute to nonadherence in older individuals. Although modification of most of these factors is challenging, optimizing the dimensions, palatability, and appearance of drug products is a key intervention to reduce nonadherence. Manufacturers play a pivotal role in ensuring that these patient-centric drug products are tailored to the practical challenges encountered by older individuals, facilitating visual identification and swallowability. Additionally, medical providers and pharmacists are crucial in ensuring the appropriate prescription and dispensing of these patient-centric formulations (Shariff *et al*., 2020).

The ability of patients to adhere to prescribed therapy may hinge on specific skills and capabilities. When lacking, patients might modify their approach, leading to inappropriate drug use, incorrect administration, suboptimal adherence, or even discontinuation of medication therapy. Some individuals, in such situations, may rely on assistance from caregivers to handle their medications. Managing medications generally becomes more challenging as the number of drug products, dosage forms, and dosing schedules increases. This complexity likely contributes to variations in the safety and efficacy of a drug in real-world patient's post-product launch, compared to the outcomes observed in well-controlled clinical trials (Stegemann *et al*., 2016).

This potential disparity is not unexpected, considering that most randomized clinical trials (RCT) primarily focus on evaluating the efficacy and safety profiles of drugs for treating chronic conditions in relatively homogeneous patient samples, often excluding individuals with relevant co-morbidities, disabilities, and impairments (Cerreta *et al*., 2012). The assessment of risks and benefits in drug treatment is thus based on the average effects observed in these randomized patient populations, potentially overlooking the variability in responsiveness to treatment and susceptibility to adverse effects across all patients and patient groups for whom the drug will be prescribed post-approval. The resulting approved drug product may not offer the desired individual risk/benefit profile, emphasizing the need to consider this risk in the overall therapeutic decision-making process regarding the patient's acceptance and success with a specific drug therapy (Tinetti *et al*., 2011; Eichler *et al*., 2011).

1.5.1 Factors Affecting Patients' Preferences in Dosage Forms

Patient preferences regarding dosage forms can be impacted by a range of factors, reflecting their individual needs, choices, and lifestyle considerations. A comprehensive understanding of these factors is essential for pharmaceutical developers, healthcare providers, and policymakers to formulate medications that are not only effective but also well-received by patients. Here are key factors influencing patients' preferences in dosage forms:

i. **Ease of Administration**: Patient preferences are significantly influenced by the convenience and simplicity of administering a medication. Dosage forms that are

easy to swallow, require minimal preparation, or incorporate user-friendly administration devices are often favored. This consideration is particularly crucial for patients facing challenges in handling complex dosage forms due to their medical conditions (Menditto *et al*., 2020).

ii. **Taste and Odor**: Sensory attributes, including taste and odor, play a pivotal role in patients' acceptance of medications. Unpleasant taste or smell can lead to aversion, especially among pediatric and geriatric populations. Efforts to enhance the palatability of liquid formulations or mask the taste of oral medications can contribute to improved patient satisfaction (Davies *et al*., 2008; Bunupuradah *et al*., 2006).

iii. **Dosage Frequency**: Patients' preferences can be influenced by the frequency with which a medication needs to be taken. Some may prefer once-daily dosing for convenience and better adherence, while others may find multiple daily doses more manageable. Extended-release formulations with less frequent dosing may be particularly appealing to those seeking convenience (Paes *et al*., 1997; Claxton *et al*., 2001).

iv. **Size and Shape of Dosage Form**: Physical characteristics, such as the size and shape of a dosage form, can impact patient preferences. Smaller, easily swallowable tablets or capsules are often preferred over larger or awkwardly shaped ones, especially for individuals with swallowing difficulties or an aversion to large pills (Menditto *et al*., 2020).

v. **Cultural and Personal Beliefs**: Cultural factors can shape patients' preferences, with some cultures favoring specific herbal remedies or traditional dosage forms. Additionally, individual beliefs and attitudes toward medications, including preferences for natural or synthetic formulations, can influence patient choices (Chia *et al*., 2006).

vi. **Patient Age and Demographics**: Age and demographic factors play a role in dosage form preferences. Pediatric patients may prefer liquid formulations or chewable tablets, while older adults may find orally disintegrating tablets or liquid forms more suitable. Preferences may also be influenced by specific health conditions or disabilities (Rolnick *et al*., 2013).

vii. **Accessibility and Affordability**: The accessibility and affordability of certain dosage forms can impact patient preferences. Patients may prefer medications that are readily available, affordable, and covered by insurance or healthcare programs. The availability of generic forms may also influence choices (Matsui 2013).

viii. **Patient Involvement in Decision-Making**: Actively involved patients in their healthcare decisions may have stronger preferences for specific dosage forms. Shared decision-making allows patients to express their preferences, ensuring that the chosen dosage form aligns with their lifestyle and preferences (Menditto *et al*., 2020).

ix. **Experience with Previous Medications**: Past experiences with medications can shape patients' preferences. Positive encounters with a particular dosage form may lead to a preference for similar formulations, while negative experiences may result in aversions to certain forms (Ibrahim *et al*., 2021).

x. **Psychological and Emotional Factors**: Patient perceptions of the dosage form's safety, efficacy, and overall acceptability can be influenced by psychological and emotional factors. Some patients may feel more comfortable with familiar dosage forms, while others may be open to trying innovative formulations (Bak-Sosnowska *et al*., 2021).

i.

1.6 Background of the Study

The rationale for this study centers on the decreased efficacy of medications in treating diseases due to patients requiring assistance in adhering to prescribed medications from healthcare providers. Patient adherence is vital for successful medical treatments, posing a challenge when patients are excluded from medication decisions. Medication efficacy relies on plasma levels, where each dose increases concentration to reach maximal plasma levels for optimal effects. Dosage formulations play a pivotal role in medication adherence, influencing patients' ability and willingness to follow treatment plans. Key aspects impacting medication adherence include the physical form, taste, understanding, compliance, physical characteristics, psychosocial factors, cost, and storage and stability problems.

Factors like difficulty swallowing, frequent dosing, taste preferences, psychosocial stigma, medication visibility, cost, and stability impact patient adherence and overall efficacy.

1.7 Significance of the Study

The healthcare system is undergoing a significant transformation, shifting away from the traditional emphasis solely on medications. This change is encapsulated in the proposed study, challenges due to pharmaceutical dosage form design and its effects on patient choices and compliance." The aim of this study is to elaborate on the importance of reshaping patient care, with healthcare professionals increasingly focusing on patient-centered care. Patient-centered care recognizes the crucial role of actively involving patients in decisions related to their healthcare and medications, tailoring medical treatment to address individual needs, preferences, and values. By implementing patients' choices, a sense of trust is established, as patients perceive that their perspectives are valued and taken into consideration.

1.8 Aim and Objectives of the Study

To investigate and understand the challenges due to pharmaceutical dosage form design and its effects on patient choices and compliance. The study aims to provide valuable insights into the relationship between dosage formulation challenges and patient choices, with the ultimate goal of contributing to the development of more patient-friendly medications and improving overall treatment adherence and outcomes.

The objectives of the study are:

i. To evaluate public knowledge and evaluate dosage form preferences among adult participants.
ii. To Assess Patient Preferences and Choices
iii. To demonstrate the association of the respondent demographic variables and dosage form preference.

iv. To provide recommendations for improvement

CHAPTER TWO

2.0 RESEARCH METHODOLOGY

The techniques and processes used in this study are explained in this chapter. Study design and setting, population, sample size, data collection instrument and administration and also the method of data analysis are all included in this chapter.

2.1 Study Design and Setting

No specific sampling technique was used except that the pre-tested standardized questionnaire was converted to Google form and distributed to various social media platforms including Instagram, X, WhatsApp and Facebook in March, 2024.The study's methodology enabled the collection of quantitative and qualitative data, resulting in a comprehensive understanding of the various challenges that patient face which influence that choice of dosage form and possible compliance issues. Following informed consent of participants, a structured online questionnaire was used to collect the following information from each study participant; socio-demographics, prior knowledge of dosage forms, patient's choices regarding dosage forms and recommendations of the use of dosage forms.

2.2 Study Participants

The study was carried out through an online questionnaire using Google forms, and involved general population with the following inclusion and exclusion criteria;

Inclusion criteria

- Adult respondents from ages 16 and above who had sufficient knowledge about the internet and could respond to them

Exclusion criteria

- Adults who had no access to google or the internet
- Adults who had psychiatric disorders
- Adults who had disability in their hands

2.3 Sample Size

The sample size for this study was 505 with a response rate of 100%

2.4 Data Collection

Google forms was used to create a standardized online questionnaire which was able to accurately and efficiently collect needed information from participants over a period of one month. The questions in the online questionnaire were in four broad sections: socio-demographic data, prior knowledge of dosage forms which comprises of seven (7) domains, patient's choices regarding dosage forms comprising of four (4) domains and recommendations of the use of dosage forms.

2.5 Data Analysis

The data obtained were sorted and processed by assigning codes and inputting into excel spreadsheet. Descriptive analysis was done on the data and interpreted. The information was presented in the form of tables. Percentages, mean and standard deviation were calculated for.

QUESTIONNAIRE

Dosage Formulation challenges and their effects on Patient's choices

Dear Participant,

We appreciate your valuable time in contributing my research on dosage formulation challenges and its impact on patient choices. Your feedback is crucial in enhancing our understanding of the experiences and preferences of healthcare professionals and patients.

Objective:

This questionnaire aims to explore the challenges associated with dosage formulations and how these challenges influence the decisions and choices made by both healthcare professionals and patients.

Confidentiality:

Your responses are confidential, and the information provided will only be used for research purposes. Your participation is voluntary, and you may withdraw at any time.

Instructions: Please answer each question thoughtfully and honestly. If a question does not apply to you, feel free to skip it. Your feedback will contribute to advancements in dosage formulation strategies and, ultimately, improve patient care.

Thank you for your participation.

Sincerely,

Researcher.

SECTION A: SOCIODEMOGRAPHIC CHARACTERISTICS OF RESPONDENTS

1. **Age** (**Years**): Below 20 [ ], 20-30[ ], 31-40 [ ], Above 40 [ ]
2. **Marital status**: Single [ ], Married [ ]
3. **Educational status**: Primary[ ], Secondary[ ], Tertiary[ ], None[ ]
4. Religion: Christian [ ], Muslim [ ] African Traditional Religion (ATR) [ ], Other _____
5. Occupation: _____

6. Income (per month): Below 30k[ ], 30-50k [ ], 50-75k [ ], 75-100k [ ], 100-150k[ ], Above 150k [ ],

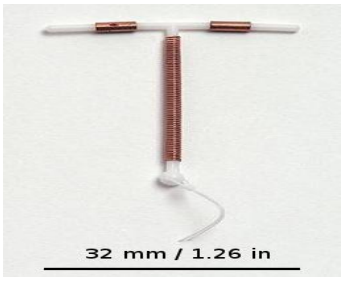
SECTION B: PRIOR KNOWLEDGE ON DOSAGE FORMS

Answer each questions as it applies to you.

7. Do you know what dosage forms/formulations are? Yes [ ], No [ ], Maybe [ ]
8. Have you used any medication to treat an illness before? Yes [ ], No [ ],
9. Which of these dosage forms did you use?

Tablets/Capsules [ ]

Syrups/Liquids [ ]



Implants [ ]

Inhaler [ ]

Creams [ ]

Inserts/Suppositories [ ]

Injections [ ]

Other:_____

10. How satisfied are you with the current dosage formulations? Very Satisfied [ ], Not Satisfied [ ], There could be improvements [ ],
11. Have you ever suggested to be given a particular dosage form over another? Yes [ ], No [ ]
12. If your answer to the previous question was yes, which dosage form did you request for and which dosage form were you given? _____
13. Do you feel a certain dosage form works better for you than another? If yes, which? _____

SECTION C: PATIENT'S CHOICES REGARDING DOSAGE FORMS

Answer as it applies to you

14. Have you ever faced challenges in administering or consuming your medications? Yes [ ], No [ ],
15. Which of these dosage formulation challenges did you face? The medication was too large [ ], It was too bitter [ ], The tablet count was too much [ ], The smell was bad [ ], The cost was too expensive [ ],
16. Would you say any of those problems you marked above has prevented you from finishing the medications prescribed to you by your doctor? Yes [ ], No [ ],
17. Have you ever switched medications due to dissatisfaction with the dosage form?

SECTION D: RECOMMENDATIONS

18. What are your recommendations for improving the use of other dosage forms of medicines? _____

Appreciation Message

19. Thank you very much for participating in my survey. Your input would be of great contribution to the healthcare sector. Yes [ ], No [ ]

3.0 CHAPTER THREE

3.1 Results

505 respondents participated in this study; the characteristic demographics of these respondents are present in Table 1. Table 2, 3 and 4 shows the prior knowledge of the patient on dosage forms, the patient's choices on dosage form and association between patient's characteristics and dosage form preference respectively.

Table 1a: Demographics of study participants

Majority of the participants fall within the 20-30 age range (75.6%) and are predominantly single (89.5%). Tertiary education was prevalent among participants (92.7%), with the majority of the participants also identifying as Christians (83.9%).

S/N	Variable	Frequency	Percent (%)
1	Age		
	Below 20 Years	67	13.3
	20-30 Years	382	75.6
	31-40 Years	35	6.9
	Above 40 Years	21	4.2
	Total	505	100.0
2	Marital Status		
	Single	452	89.5
	Married	53	10.5
	Total	505	100.0
3	Educational Status		
	Primary	3	.6
	Secondary	23	4.6
	Tertiary	468	92.7

	None	11	2.2
	Total	505	100.0
4	Religion		
	Christian	425	83.9
	Muslim	69	13.7
	African Traditional Religion (ATR)	11	2.2
	Nil	1	.2
	Total	505	100.0

Table 1b: Demographics of study participants

Students constituted the largest occupational group, comprising 49.9%, and income distribution exhibited variability (Below 30,000naira the most prevalent at 30.7%).

S/N	Variable	Frequency	Percent (%)
5	Occupation		
	Student	252	49.9
	Self Employed	148	29.3
	Employed	94	18.6
	Unemployed	11	2.2
	Total	505	100.0
6	Income (Per Month)		
	Below 30k	155	30.7
	30-50k	93	18.4
	50-75k	42	8.3
	75k-100k	31	6.1
	100k-150k	38	7.5
	Above 150k	107	21.2
	Total	505	100.0

Table 2a: Prior Knowledge on Dosage Forms

A significant 73.7% of participants showed knowledge of dosage forms. 98.8% of the participants had prior experience using medications, with the combination of tablet/capsules/syrups/liquids/creams/injection being the most common dosage forms at 34.9%.

S/N	Variable	Frequency	Percent (%)
1	Do You Know What Dosage Forms/Formulations Are?		
	Yes	372	73.7
	No	85	16.8
	Maybe	48	9.5
	Total	505	100.0
2	Have You Used Any Medication to Treat an Illness Before?		
	Yes	499	98.8
	No	6	1.2
	Total	505	100.0
3	Which Of These Dosage Forms Did You Use?		
	Tablets/Capsules	52	10.3
	Syrups/Liquids	3	.6
	Injections	6	1.2
	Insert/Suppositories	1	.2
	Tablets/Capsules; Syrups/Liquids; Liquids	21	4.2
	Tablets/Capsules; Syrups/Liquids; Inhaler; Creams; Inserts/Suppositories; Injections	20	4.0
	Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections; Eyedrops	2	.4
	Inhaler	1	.2

Tablets/Capsules; Syrups/Liquids; Creams; Injections	176	34.9
Syrups And Liquids	2	.4
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections	73	14.5
Tablets/Capsules; Syrups/Liquids; Liquids	21	4.2
Tablets/Capsules; Syrups/Liquids; Inhaler; Creams; Inserts/Suppositories; Injections	20	4.0
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections; Eyedrops	2	.4
Tablets/Capsules; Syrups/Liquids; Implants; Inhaler; Creams; Inserts/Suppositories; Injections	58	11.5
Tablets/Capsules; Syrups/Liquids; Injections	69	13.7
Tablets/Capsules; Creams; Injections	20	4.0
Total	505	100.0

Table 2b: Prior Knowledge on Dosage Forms

Satisfaction levels varied, with 54.9% expressing contentment with current formulations, while 40.4% identified areas for improvement. 56.6% of the participants actively suggested a particular dosage form.

S/N	Variable	Frequency	Percent (%)
4	How Satisfied Are You with The Current Dosage Formulations?		
	Very Satisfied	275	54.9
	Not Satisfied	24	4.8
	There Could Be Improvements	204	40.4
	Total	505	100.0
5	Have You Ever Suggested to Be Given a Particular Dosage Form Over Another?		
	Yes	286	56.6
	No	216	42.8
	Total	505	100.0

Table 3: Patient's Choices Regarding Dosage Forms

79.2% of participants faced challenges in medication administration or consumption. Of those challenges, 69.3% reported instances where the challenges sometimes prevented the completion of prescribed medications. 47.7% of participants reported to have switched medications due to dissatisfaction with dosage forms. Challenges reported included medication size (12.7%), bitterness (11.7%), excessive tablet count (5.9%), bad smell (8.1%), and cost (5.7%). Combinations of challenges were prevalent, with that of bitterness, excessive tablet count, and bad smell being the most common at 13.7%.

S/N	Variable	Frequency	Percent (%)
1	Have You Ever Faced Challenges in Administering or Consuming Your Medications?		
	Yes	400	79.2
	No	105	20.8
	Total	505	100.0
2	Would You Say Any of Those Problems You Marked Above Has Prevented You from Finishing the Medications Prescribed to You by Your Doctor?		
	Yes	360	69.3
	No	145	28.7
	Total	505	100.0
3	Have You Ever Switched Medications Due to Dissatisfaction with the Dosage Form?		
	Yes	241	47.7
	No	264	52.3
	Total	505	100.0

4	Which Of These Dosage Formulation Challenges Did You Face?		
	The Medication Was Too Large	64	12.7
	It Was Too Bitter	59	11.7
	The Tablet Count Was Too Much	30	5.9
	The Smell Was Bad	41	8.1
	The Cost Was Too Expensive	29	5.7
	It Was Too Bitter; The Tablet Count Was Too Much	23	4.6
	It Was Too Bitter; The Smell Was Bad	13	2.6
	The Medication Was Too Large; It Was Too Bitter; The Tablet Count Was Too Much; The Smell Was Bad	69	13.7
	It Was Too Bitter; The Tablet Count Was Too Much; The Smell Was Bad; The Cost Was Too Expensive	24	4.8
	E Medication Was Too Large; It Was Too Bitter; The Tablet Count Was Too Much; The Smell Was Bad; The Cost Was Too Expensive	41	8.1
	It Was Too Bitter; The Tablet Count Was Too Much; The Smell Was Bad	112	22.2
	Total	505	100.0

Table 4a: Association of the respondent demographic variables and dosage form preference (Age and dosage form preference)

Dosage form preference	Below 20years	20-30 years	31-40 years	Above 40 years	Total	P-Value
Age						
Tablets/Capsules; Syrups/Liquids; Liquids	2	18	1	1	21	
Tablets/Capsules; Syrups/Liquids; Inhaler; Creams; Inserts/Suppositories; Injections	0	16	2	2	20	
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections; Eyedrops	0	0	1	1	2	
Inhaler	1	0	0	0	1	
Tablets/Capsules; Syrups/Liquids; Creams; Injections	26	136	10	4	176	0.000
Liquids/syrups	0	2	0	0	2	
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections	8	61	3	1	73	
Tablets/Capsules	13	32	4	3	52	
Inserts/ suppositories	0	0	1	0	1	
Syrups/Liquids	0	2	0	1	3	

Tablets/Capsules; Syrups/Liquids; Implants; Inhaler; Creams; Inserts/Suppositories; Injections	6	46	4	2	58
Injections	0	4	1	1	6
Tablets/Capsules; Syrups/Liquids; Injections	10	52	4	3	69
Tablets/Capsules; Creams; Injections	2	13	4	1	20
Total	66	382	35	21	505

Table 4b: Association of the respondent demographic variables and dosage form preference (Marital status and dosage preference)

Dosage form preference	Single	Married	Total	P-Value
Marital status	0	1	1	
Tablets/Capsules; Syrups/Liquids; Liquids	18	3	21	
Tablets/Capsules; Syrups/Liquids; Inhaler; Creams; Inserts/Suppositories; Injections	16	4	20	
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections; Eyedrops	1	1	2	
Inhaler	1	0	1	
Tablets/Capsules; Syrups/Liquids; Creams; Injections	164	12	176	
Liquids/syrups	2	0	2	0.203
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections	70	3	73	
Tablets/Capsules	45	7	52	
Inserts/ suppositories	1	0	1	
Syrups/Liquids	2	1	3	
Tablets/Capsules; Syrups/Liquids; Implants; Inhaler; Creams;	52	6	58	

Inserts/Suppositories; Injections			
Injections	4	2	6
Tablets/Capsules; Syrups/Liquids; Injections	60	9	69
Tablets/Capsules; Creams; Injections	16	4	20
Total	452	53	505

Table 4c: Association of the respondent demographic variables and dosage form preference (Educational status and dosage preference)

Dosage form Preference	Primary	Secondary	Tertiary	None	Total	P-Value
Educational status	0	0	1	0	1	
Tablets/Capsules; Syrups/Liquids; Liquids	0	1	20	0	21	
Tablets/Capsules; Syrups/Liquids; Inhaler; Creams; Inserts/suppositories; Injections	0	0	19	1	20	
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections; Eyedrops	0	0	2	0	2	
Inhaler	0	0	1	0	1	
Tablets/Capsules; Syrups/Liquids; Creams; Injections	2	14	157	3	176	
Liquids/syrups	0	0	2	0	2	
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections	0	2	69	2	73	1.000
Tablets/Capsules	0	2	50	0	52	
Inserts/ suppositories	0	0	1	0	1	
Syrups/Liquids	0	0	3	0	3	
Tablets/Capsules; Syrups/Liquids; Implants;	1	1	54	2	58	

Inhaler; Inserts/suppositories; Injections	Creams;					
Injections		0	0	6	0	6
Tablets/Capsules; Syrups/Liquids; Injections		1	1	64	3	69
Tablets/Capsules; Injections	Creams;	0	1	19	0	20
Total		4	22	468	11	505

Table 4d: Association of the respondent demographic variables and dosage form preference (Religion and dosage preference)

Dosage form preference / Religion	Christian	Muslim	African Traditional Religion (Atr)	Nil	Total	P-Value
	1	**0**	**0**	**0**	**1**	
Tablets/Capsules; Syrups/Liquids; Liquids	17	3	1	0	21	
Tablets/Capsules; Syrups/Liquids; Inhaler; Creams; Inserts/suppositories; Injections	20	0	0	0	20	
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections; Eyedrops	2	0	0	0	2	
Inhaler	1	0	0	0	1	
Tablets/Capsules; Syrups/Liquids; Creams; Injections	142	30	4	0	176	
Liquids/syrups	2	0	0	0	2	
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections	67	6	0	0	73	0.982
Tablets/Capsules	40	10	1	1	52	
Inserts/ suppositories	1	0	0	0	1	
Syrups/Liquids	3	0	0	0	3	
Tablets/Capsules; Syrups/Liquids; Implants; Inhaler; Creams; Inserts/suppositories; Injections	52	4	2	0	58	
Injections	5	1	0	0	6	

Tablets/Capsules; Syrups/Liquids; Injections	56	11	2	0	69
Tablets/Capsules; Creams; Injections	15	4	1	0	20
Total	424	69	11	1	505

Table 4e: Association of the respondent demographic variables and dosage form preference (Occupation and dosage preference)

Dosage form Preference / Occupation	Student	Self Employed	Employed	Unemployed	Total	P-Value
Tablets/Capsules; Syrups/Liquids; Liquids	11	7	3	0	21	
Tablets/Capsules; Syrups/Liquids; Inhaler; Creams; Inserts/suppositories; Injections	8	5	7	0	20	
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections; Eyedrops	0	0	2	0	2	
Inhaler	1	0	0	0	1	
Tablets/Capsules; Syrups/Liquids; Creams; Injections	104	38	29	6	176	0.533
Liquids/syrups	2	0	0	0	2	
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections	36	25	11	1	73	
Tablets/Capsules	30	16	5	1	52	
Inserts/ suppositories	0	1	0	0	1	
Syrups/Liquids	0	2	1	0	3	
Tablets/Capsules; Syrups/Liquids; Implants; Inhaler; Creams;	24	19	15	0	58	

Inserts/suppositories; Injections					
Injections	3	2	1	0	6
Tablets/Capsules; Syrups/Liquids; Injections	25	27	15	2	69
Tablets/Capsules; Creams; Injections	9	6	4	1	20
Total	252	148	94	11	505

Table 4f: Association of the respondent demographic variables and dosage form preference (Income per month and dosage preference)

Dosage form Preference / Income	Below 30k	30-50k	50-75k	75-100k	100-150k	Above 150k	Total	P-Value
Tablets/Capsules; Syrups/Liquids; Liquids	6	7	2	3	0	3	21	
Tablets/Capsules; Syrups/Liquids; Inhaler; Creams; Inserts/suppositories; Injections	3	6	2	1	1	7	20	
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections; Eyedrops	0	0	0	0	1	1	2	
Inhaler	1	0	0	0	0	0	1	
Tablets/Capsules; Syrups/Liquids; Creams; Injections	78	30	13	8	9	38	176	
Liquids/syrups	0	1	0	0	0	0	2	0.020
Tablets/Capsules; Syrups/Liquids; Cream; Inserts/Suppositories; Injections	24	16	5	7	5	16	73	
Tablets/Capsules	26	8	3	2	5	8	52	
Inserts/ suppositories	0	0	0	1	0	0	1	
Syrups/Liquids	0	0	1	0	1	1	3	
Tablets/Capsules; Syrups/Liquids; Implants;	18	13	5	4	6	12	58	

Inhaler; Creams; Inserts/suppositories; Injections							
Injections	1	2	1	0	2	0	6
Tablets/Capsules; Syrups/Liquids; Injections	27	6	8	5	6	17	69
Tablets/Capsules; Creams; Injections	8	4	2	0	2	4	20
Total	194	93	42	31	38	107	505

3.2 Discussion

Various factors are present that can impact medication adherence and lead to failed drug therapy such as stability and shelf life of the drug, dosage regimen and even the dosage form of the drug and some drug characteristics especially those in oral dosage forms, considerations such as taste and palatability can significantly influence the adherence to medications for individuals (Lucas *et al*., 2004; Ternik *et al*., 2018; Homayun *et al*., 2019).

3.2.1 Demographic Characteristics

The demographic data in Table 1 showed the majority of the participants to be young adults. The majority of participants falling within the 20-30 age range (75.6%) could be due to the fact that the target research group were university students. This is further supported by the data showing a higher prevalence of tertiary education among the respondents (92.7%). The prevalence of tertiary education (92.7%) among participants reflects the growing influence of education on health literacy and decision-making (Berkman *et al*., 2000). The dominance of Christians (83.9%) among participants resonates with cultural considerations in healthcare choices highlighted by Trinitapoli and Yeatman (2008). The occupational distribution, with students as the largest group (49.9%), correlates with studies emphasizing the role of occupation in shaping healthcare decisions and medication adherence particularly (Tomar *et al*., 2019). Variability in income distribution (Below 30,000 Naira most prevalent at 30.7%) echoes economic factors impacting healthcare choices as discussed by Hommell (2020).

3.2.2 Patient Knowledge on Dosage Forms and Prior Medication Experience/Choices

The study reveals that a significant portion (73.7%) of participants possesses knowledge of dosage forms. This aligns with the emphasis on patient education and supports the World Health Organization's guidelines on patient empowerment through education as reported also by Samoocha *et al*. (2010).

The overwhelming majority (98.8%) of participants having prior experience with medications underscores the prevalence of medication usage in the studied population. The combination of tablet/capsules/syrups/liquids/creams/injections as the most common dosage forms (34.9%) reflects the multifaceted nature of clinical practice. This bears similarities to Alyami *et al*.'s (2017) research on young adults' dosage form preferences. The study revealed a strong preference for oral disintegrating tablets as the primary choice (58%), followed by liquids (20%), capsules (12%), and tablets (11%). Participants favored colors like pink or white and showed a preference for small-sized dosage forms (<8 mm) with a round shape. Strawberry was the top choice for flavor (30.8%), while orange was the least preferred (5.8%). Additionally, the research emphasized the significance of specific physical attributes in orally disintegrating tablets (ODTs), ranking disintegration time as the most crucial, followed by taste, size, and flavor, in that order. This therefore explains that dosage form characteristics greatly impact patient's preference. From the results of the study, satisfaction levels varied, with 54.9% expressing contentment with current formulations and 40.4% identifying areas for improvement.

A significant proportion (79.2%) of participants faced challenges in medication administration or consumption. Of those challenges, 69.3% of the participants reported instances where the challenges sometimes prevented the completion of prescribed medications. Challenges reported included medication size (12.7%), bitterness (11.7%), excessive tablet count (5.9%), bad smell (8.1%), and cost (5.7%). Combinations of challenges were prevalent, with bitterness, excessive tablet count, and bad smell being the most common at 13.7%. This is corroborated by the research conducted by Schiele *et al*. (2013), which revealed a notably high occurrence (37.4%) of challenges associated with swallowing solid oral dosage forms. Significantly, one out of every 11 patients reported frequent difficulties, leading many to modify their medication. Approximately one in ten of those affected exhibited non-adherence issues, underscoring the crucial need to recognize these patients and assist in their drug administration and preference for dosage forms.

3.2.3 Association between patient's demographic variables and dosage form preference

The analysis of the association between demographic variables and patients' dosage form preferences reveals interesting insights. In terms of age (Table 4a), participants aged 20-30 years displayed a significant preference for Tablets/Capsules; Syrups/Liquids; Creams; Injections (p-value=0.000). However, the other age groups exhibited varying preferences with statistically significant associations (p-value<0.05) for specific dosage forms. Marital status (Table 4b) did not show a statistically significant association (p-value=0.203) with dosage form preference, indicating that this factor might not play a significant role in shaping patients' preferences.

Similarly, educational status (Table 4c) demonstrated no significant association (p-value=1.000) with dosage form preference, suggesting that patients' educational backgrounds may not be a decisive factor in determining their preferences. Religion (Table 4d) also exhibited no statistically significant association (p-value=0.982) with dosage form preference, highlighting the diversity in preferences across different religious groups. Occupation (Table 4e) did not show a significant association (p-value=0.533), indicating that preferences are varied among students, self-employed, employed, and unemployed individuals.

However, income per month (Table 4f) demonstrated a statistically significant association (p-value=0.020) with dosage form preference, suggesting that individuals with different income levels may have distinct preferences for specific dosage forms. Overall, these findings underscore the complexity of factors influencing dosage form preferences, emphasizing the importance of personalized approaches in medication formulations to cater to the diverse needs of patient populations.

4.0 CHAPTER FOUR

4.1 Conclusion

In conclusion, patient knowledge on dosage forms and prior medication experiences revealed a high level of awareness among participants, emphasizing the importance of patient education in promoting medication adherence. The diverse preferences for specific dosage forms, as highlighted by Alyami *et al*.'s (2017) research on young adults, underscore the need for personalized medication formulations that consider factors such as color, size, shape, and flavor. Satisfaction levels varied, with a substantial portion of participants expressing contentment but also identifying areas for improvement.

Challenges in medication administration or consumption were prevalent, with a significant proportion facing obstacles that sometimes hindered the completion of prescribed medications. Notably, challenges like medication size, bitterness, excessive tablet count, odour, and cost were reported, with combinations of these challenges being common. The study aligns with Schiele *et al*.'s (2013) findings, which emphasized on the high occurrence of difficulties associated with swallowing solid oral dosage forms and the subsequent impact on medication adherence.

The analysis of the association between demographic variables and dosage form preferences yielded intriguing insights. While age exhibited statistically significant associations with specific dosage forms, other demographic factors like marital status, educational background, religion, and occupation demonstrated varying preferences without clear associations. Notably, income per month showed a statistically significant association with dosage form preference, suggesting the influence of economic factors on patients' choices.

In essence, this research underscores the importance of considering diverse demographic factors and individual preferences in designing and formulating medications. A personalized approach, acknowledging the unique challenges and preferences of patients, is crucial in enhancing medication adherence, overall patient satisfaction, and, ultimately, healthcare

outcomes. The findings contribute to the growing body of knowledge aimed at improving pharmaceutical formulations and healthcare strategies for diverse patient populations.

4.2 Limitations of the Study

The study conducted through an online Google Form, while yielding valuable insights into dosage formulation challenges and patient preferences, is accompanied by several limitations. The online survey methodology introduces a potential sampling bias, as participants more accustomed to digital platforms may be overrepresented, potentially skewing the findings. This raises concerns about the generalizability of the results to individuals who are less tech-savvy or lack consistent internet access. Moreover, the digital nature of the survey may contribute to the digital divide, excluding those without regular access to the internet or digital devices, particularly impacting older adults or individuals from lower socioeconomic backgrounds.

A significant limitation lies in the potential self-selection bias inherent in online surveys. Participants who voluntarily chose to engage in the survey may possess distinct characteristics compared to those who opted out, introducing a potential source of bias. Additionally, the lack of direct control over respondents' environments during the online survey compromised data reliability. Factors such as distractions or incomplete participant focus influence the quality of responses.

Another critical constraint is the absence of immediate interaction characteristic of in-person interviews or focus groups and the inability to clarify ambiguous responses or ensure a uniform understanding of survey questions, potentially introducing uncertainties into the collected data. The reliance on online platforms may also impact response quality, as participants may feel less accountable compared to traditional survey settings.

The study's scope might be limited due to its online format, hindering the exploration of certain aspects related to dosage form preferences. The inability to physically present dosage forms to participants may have restricted a nuanced understanding of their choices. Furthermore, the study's focus on online responses assumes a certain level of digital literacy

among participants, potentially disenfranchising those less familiar with online surveys or uncomfortable with technology.

An additional concern revolves around the inability to verify respondent identity in online surveys, creating the possibility of duplicate responses or entries from individuals outside the intended target population. This lack of identity verification could compromise the integrity of the collected data. Finally, the study's online format might not adequately account for cross-cultural nuances, potentially limiting its generalizability across diverse cultural contexts.

In acknowledging these limitations, it becomes evident that the study's findings should be interpreted within the context of these constraints. Addressing these challenges in future research endeavors is essential to refining methodologies and ensuring a more comprehensive understanding of dosage formulation challenges and patient preferences.

REFERENCES

Afrin, S. and Gupta, V., 2020. Pharmaceutical formulation.

Aggarwal, G. and Dhawan, S., 2009. Development, fabrication and evaluation of transdermal drug delivery system-a review Pharm.

Ahmed, M.M. and Ali, M.M., 2016. SEMISOLID DOSAGE FORM: TOPICAL GEL FORMULATION A.

Alagusundaram, M., Deepthi, N., Ramkanth, S., Angalaparameswari, S., Saleem, T.M., Gnanaprakash, K., Thiruvengadarajan, V.S. and Chetty, C.M., 2010. Dry powder inhalers-an overview. *Int. J. Res. Pharm. Sci*, *1*(1), pp.34-42.

Allen, L. and Ansel, H.C., 2013. *Ansel's pharmaceutical dosage forms and drug delivery systems*. Lippincott Williams & Wilkins.

Alvarez-Lorenzo, C. and Concheiro, A., 2013. From drug dosage forms to intelligent drug-delivery systems: a change of paradigm. In *Smart materials for drug delivery* (pp. 1-32). The Royal Society of Chemistry.

Alyami, H., Dahmash, E., Alyami, F., Dahmash, D., Huynh, C., Terry, D. and Mohammed, A.R., 2017. Dosage form preference consultation study in children and young adults: paving the way for patient-centred and patient-informed dosage form development. *European Journal of Hospital Pharmacy*, *24*(6), pp.332-337.

American Society of Hospital Pharmacists. (1987). *Handbook on Extemporaneous Formulations*. Bethesda, MD.

Aston, L., Hilton, A., Moutela, T., Shaw, R. and Maidment, I., 2017. Exploring the evidence base for how people with dementia and their informal carers manage their medication in the community: a mixed studies review. *BMC geriatrics*, *17*(1), pp.1-11.

Aulton, M.E. and Taylor, K. eds., 2013. *Aulton's pharmaceutics: the design and manufacture of medicines*. Elsevier Health Sciences.

Bąk-Sosnowska, M., Wyszomirska, J. and Daniel-Sielańczyk, A., 2021. Selected psychological factors and medication adherence in patients with rheumatoid arthritis. *Reumatologia/Rheumatology*, *59*(2), pp.90-97.

Barry, P.W. and O'Callaghan, C., 2003. The influence of inhaler selection on efficacy of asthma therapies. *Advanced drug delivery reviews*, *55*(7), pp.879-923.

Berkman, L.F. and Glass, T., 2000. Social integration, social networks, social support, and health. *Social epidemiology*, *1*(6), pp.137-173.

Bunupuradah, T., Wannachai, S., Chuamchaitrakool, A., Intasan, J., Nuchapong, T., Neiss, W., Kramm, K., Pancharoen, C., Burger, D. and Ananworanich, J., 2006. Use of taste-masking product, FLAVORx, to assist Thai children to ingest generic antiretrovirals. *AIDS Research and Therapy*, *3*, pp.1-5.

Cerreta, F., Eichler, H.G. and Rasi, G., 2012. Drug policy for an aging population—the European Medicines Agency's geriatric medicines strategy. *New England Journal of Medicine*, *367*(21), pp.1972-1974.

Chauhan, L. and Gupta, S., 2020. Creams: A review on classification, preparation methods, evaluation and its applications. *Journal of drug delivery and therapeutics*, *10*(5-s), pp.281-289.

Chia, L., Schlenk, E.A. and Dunbar-Jacob, J., 2006. Effect of personal and cultural beliefs on medication adherence in the elderly. *Drugs & aging*, *23*, pp.191-202.

Claxton, A.J., Cramer, J. and Pierce, C., 2001. A systematic review of the associations between dose regimens and medication compliance. *Clinical therapeutics*, *23*(8), pp.1296-1310.

Cramer, M.P. and Saks, S.R., 1994. Translating safety, efficacy and compliance into economic value for controlled release dosage forms. *Pharmacoeconomics*, *5*, pp.482-504.

Davies, E.H. and Tuleu, C., 2008. Medicines for children: a matter of taste. *The Journal of pediatrics*, *153*(5), pp.599-604.

Dhiman, S., Singh, T.G. and Rehni, A.K., 2011. Transdermal patches: a recent approach to new drug delivery system. *Int J Pharm Pharm Sci*, *3*(5), pp.26-34.

Dolovich, M.B., Ahrens, R.C., Hess, D.R., Anderson, P., Dhand, R., Rau, J.L., Smaldone, G.C. and Guyatt, G., 2005. Device selection and outcomes of aerosol therapy: evidence-based guidelines: American College of Chest Physicians/American College of Asthma, Allergy, and Immunology. *Chest*, *127*(1), pp.335-371.

Drumond, N., van Riet-Nales, D.A., Karapinar-Çarkit, F. and Stegemann, S., 2017. Patients' appropriateness, acceptability, usability and preferences for pharmaceutical preparations: Results from a literature review on clinical evidence. *International journal of pharmaceutics*, *521*(1-2), pp.294-305.

Eichler, H.G., Abadie, E., Breckenridge, A., Flamion, B., Gustafsson, L.L., Leufkens, H., Rowland, M., Schneider, C.K. and Bloechl-Daum, B., 2011. Bridging the efficacy–effectiveness gap: a regulator's perspective on addressing variability of drug response. *Nature reviews Drug discovery*, *10*(7), pp.495-506.

Eichler, H.G., Abadie, E., Breckenridge, A., Flamion, B., Gustafsson, L.L., Leufkens, H., Rowland, M., Schneider, C.K. and Bloechl-Daum, B., 2011. Bridging the efficacy–effectiveness gap: a regulator's perspective on addressing variability of drug response. *Nature reviews Drug discovery*, *10*(7), pp.495-506.

European Medicines Agency, 2015. Good practice guide on risk minimisation and prevention of medication errors. *European Medicines Agency*.

European Medicines Agency, 2020. Reflection paper on the pharmaceutical development of medicines for use in the older population.

Frijlink, H.W., 2003. Benefits of different drug formulations in psychopharmacology. *European neuropsychopharmacology*, *13*, pp.77-84.

Garg, T., Rath, G. and Goyal, A.K., 2015. Comprehensive review on additives of topical dosage forms for drug delivery. *Drug delivery*, *22*(8), pp.969-987.

Gaur, P.K., Mishra, S., Purohit, S. and Dave, K., 2009. Transdermal drug delivery system: a review. *Asian Journal of pharmaceutical and clinical Research*, *2*(1), pp.14-20.

Gullapalli, R.P., 2010. Soft gelatin capsules (softgels). *Journal of pharmaceutical sciences*, *99*(10), pp.4107-4148.

Gutierrez, J.J.P. and Munakomi, S., 2023. Intramuscular injection. In *StatPearls [Internet]*. StatPearls Publishing.

Hammell, K.W., 2020. Making choices from the choices we have: The contextual-embeddedness of occupational choice. *Canadian Journal of Occupational Therapy*, *87*(5), pp.400-411.

Helfand, W.H. and Cowen, D.L., 1983. Evolution of pharmaceutical oral dosage forms. *Pharmacy in history*, *25*(1), pp.3-18.

Hoag, S.W., 2017. Capsules dosage form: formulation and manufacturing considerations. In *Developing solid oral dosage forms* (pp. 723-747). Academic Press.

Homayun, B., Lin, X. and Choi, H.J., 2019. Challenges and recent progress in oral drug delivery systems for biopharmaceuticals. *Pharmaceutics*, *11*(3), p.129.

Hussan, S.D., Santanu, R., Verma, P. and Bhandari, V., 2012. A review on recent advances of enteric coating. *IOSR J Pharm*, *2*(6), pp.05-11.

Ibrahim, K.M., Schommer, J.C., Morisky, D.E., Rodriguez, R., Gaither, C. and Snyder, M., 2021. The association between medication experiences and beliefs and low medication adherence in patients with chronic disease from two different societies: The USA and the Sultanate of Oman. *Pharmacy*, *9*(1), p.31.

Jackson, W.A. and Anderson, S., 2005. From electuaries to enteric coating: a brief history of dosage forms. In *Making Medicines: A Brief History of Pharmacy and Pharmaceuticals*. Pharmaceutical Press London.

Jain, K.K., 2020. An overview of drug delivery systems. *drug delivery systems*, pp.1-54.

Jaiswani, R., Prakash, A., Mishra, D.K. and Jain, D.K., 2014. Sublingual tablets: an overview. *Journal of Drug Delivery Research*, *3*(4), pp.10-21.

Kathpalia, H., Sharma, K. and Doshi, G., 2014. Recent trends in hard gelatin capsule delivery system. *J. Adv. Pharm*, *4*.

Kozarewicz, P., 2014. Regulatory perspectives on acceptability testing of dosage forms in children. *International journal of pharmaceutics*, *469*(2), pp.245-248.

Lachman, L., Lieberman, H.A. and Kanig, J.L., 1976. *The theory and practice of industrial pharmacy* . Philadelphia: Lea & Febiger. pp. 210-212

Levy, M., Duffy, C.M., Pollock, P., Budd, E., Caulfield, L. and Koren, G., 1990. Home–Based Palliative Care for Children: —Part 1: The Institution of a Program. *Journal of Palliative Care*, *6*(1), pp.11-15.

Lucas, T.I., Bishara, R.H. and Seevers, R.H., 2004. A stability program for the distribution of drug products. *Pharmaceutical Technology*, *28*, pp.68-73.

Mahato, R.I. and Narang, A.S., 2017. *Pharmaceutical Dosage Forms and Drug Delivery: Revised and Expanded*. CRC Press.

Maqbool, A., Mishra, M.K., Pathak, S., Kesharwani, A. and Kesharwani, A., 2017. Semisolid dosage forms manufacturing: Tools, critical process parameters, strategies, optimization, and recent advances. *Ind. Am. J. Pharm. Res*, *7*, pp.882-893.

Matsui, D., 2013. Medication adherence issues in patients: focus on cost. *Clinical Audit*, pp.33-42.

Mc Gillicuddy, A., Kelly, M., Crean, A.M. and Sahm, L.J., 2017. The knowledge, attitudes and beliefs of patients and their healthcare professionals around oral dosage form modification: A systematic review of the qualitative literature. *Research in Social and Administrative Pharmacy*, *13*(4), pp.717-726.

Menditto, E., Orlando, V., De Rosa, G., Minghetti, P., Musazzi, U.M., Cahir, C., Kurczewska-Michalak, M., Kardas, P., Costa, E., Sousa Lobo, J.M. and Almeida, I.F., 2020. Patient centric pharmaceutical drug product design—The impact on medication adherence. *Pharmaceutics*, *12*(1), p.44.

Nicoll, L.H. and Hesby, A., 2002. Intramuscular injection: an integrative research review and guideline for evidence-based practice. *Applied nursing research*, *15*(3), pp.149-162.

Notenboom, K., Beers, E., van Riet-Nales, D.A., Egberts, T.C., Leufkens, H.G., Jansen, P.A. and Bouvy, M.L., 2014. Practical problems with medication use that older people experience: a qualitative study. *Journal of the American Geriatrics Society*, *62*(12), pp.2339-2344.

Paes, A.H., Bakker, A. and Soe-Agnie, C.J., 1997. Impact of dosage frequency on patient compliance. *Diabetes care*, *20*(10), pp.1512-1517.

Patel, S.G. and Siddaiah, M., 2018. Formulation and evaluation of effervescent tablets: a review. *Journal of drug delivery and therapeutics*, *8*(6), pp.296-303.

Peart, J. and Clarke, M.J., 2001. New developments in dry powder inhaler technology. *American Pharmaceutical Review*, *4*, pp.37-46.

Pesko, L. J. (1993). Compounding: Oral liquids. *American Druggist*, 208, 49.

Renu, J.D., Jalwal, P. and Singh, B., 2015. Chewable Tablets: A comprehensive review. *The Pharma Innovation Journal*, *4*(5), pp.100-105.

Rolnick, S.J., Pawloski, P.A., Hedblom, B.D., Asche, S.E. and Bruzek, R.J., 2013. Patient characteristics associated with medication adherence. *Clinical medicine & research*, *11*(2), pp.54-65.

Samoocha, D., Bruinvels, D.J., Elbers, N.A., Anema, J.R. and van der Beek, A.J., 2010. Effectiveness of web-based interventions on patient empowerment: a systematic review and meta-analysis. *Journal of Medical Internet Research*, *12*(2), p.e1286.

Schiele, J.T., Quinzler, R., Klimm, H.D., Pruszydlo, M.G. and Haefeli, W.E., 2013. Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms. *European Journal of Clinical Pharmacology*, *69*, pp.937-948.

Seager, H., 1998. Drug-delivery products and the Zydis fast-dissolving dosage form. *Journal of Pharmacy and Pharmacology*, *50*(4), pp.375-382.

Seddon, G., Lounnas, V., McGuire, R., van den Bergh, T., Bywater, R.P., Oliveira, L. and Vriend, G., 2012. Drug design for ever, from hype to hope. *Journal of computer-aided molecular design*, *26*, pp.137-150.

Shariff, Z.B., Dahmash, D.T., Kirby, D.J., Missaghi, S., Rajabi-Siahboomi, A. and Maidment, I.D., 2020. Does the formulation of oral solid dosage forms affect acceptance and adherence in older patients? A mixed methods systematic review. *Journal of the American Medical Directors Association*, *21*(8), pp.1015-1023.

Snell, E.S. and Griffin, J.P., 1985. How many medicines are there? *British Medical Journal (Clinical research ed.)*, *290*(6470), p.773.

Srikrishna, S. and Cardozo, L., 2013. The vagina as a route for drug delivery: a review. *International urogynecology journal*, *24*, pp.537-543.

Stegemann, S., Ternik, R.L., Onder, G., Khan, M.A. and van Riet-Nales, D.A., 2016. Defining patient centric pharmaceutical drug product design. *The AAPS journal*, *18*, pp.1047-1055.

Stewart, K.D., Johnston, J.A., Matza, L.S., Curtis, S.E., Havel, H.A., Sweetana, S.A. and Gelhorn, H.L., 2016. Preference for pharmaceutical formulation and treatment process attributes. *Patient Preference and Adherence*, pp.1385-1399.

Ternik, R., Liu, F., Bartlett, J.A., Khong, Y.M., Tan, D.C.T., Dixit, T., Wang, S., Galella, E.A., Gao, Z. and Klein, S., 2018. Assessment of swallowability and palatability of oral dosage forms in children: report from an M-CERSI pediatric formulation workshop. *International Journal of Pharmaceutics*, *536*(2), pp.570-581.

Tinetti, M.E. and Studenski, S.A., 2011. Comparative effectiveness research and patients with multiple chronic conditions. *N Engl J Med*, *364*(26), pp.2478-81.

Tomar, S.K., Kedia, S., Singh, N., Upadhyay, A.D., Kamat, N., Bopanna, S., Yadav, D.P., Goyal, S., Jain, S., Makharia, G. and Ahuja, V., 2019. Higher education, professional occupation, and upper socioeconomic status are associated with lower adherence to medications in patients with inflammatory bowel disease. *Jgh Open*, *3*(4), pp.302-309.

Ubhe, T.S. and Gedam, P., 2020. A Brief Overview on Tablet and It's Types. *Journal of Advancement in Pharmacology*, *1*(1), pp.21-31.

United States Pharmacopeia 35–National Formulary 30. 2012. Rockville, MD: U.S. Pharmacopeial Convention.

Wahlich, J., Stegemann, S. and Orlu-Gul, M., 2013. Meeting commentary—"Medicines for older adults: Learning from practice to develop patient centric drug products". *International journal of pharmaceutics*, *456*(1), pp.251-257.

Waterman, K.C., 2011. The application of the accelerated stability assessment program (ASAP) to quality by design (QbD) for drug product stability. *AAPS PharmSciTech*, *12*, pp.932-937.

Wen, H., Jung, H. and Li, X., 2015. Drug delivery approaches in addressing clinical pharmacology-related issues: opportunities and challenges. *The AAPS journal*, *17*, pp.1327-1340.

Yeatman, S.E. and Trinitapoli, J., 2008. Beyond denomination: The relationship between religion and family planning in rural Malawi. *Demographic research*, *19*(55), p.1851.

Zhang, N.J., Terry, A. and McHorney, C.A., 2014. Impact of health literacy on medication adherence: a systematic review and meta-analysis. *Annals of Pharmacotherapy*, *48*(6), pp.741-751.