



## COMPATIBILITY STUDIES OF AZITHROMYCIN AND PARACETAMOL COMBINATION FOR THE DEVELOPMENT AS SUPPOSITORIES NOVEL DRUG DELIVERY SYSTEMS

Mahmoud Mahyoob Alburyhi<sup>1\*</sup>, Tawfeek A.A. Yahya<sup>2</sup>, Mohammed A. AlKhawlani<sup>3</sup>, Abdalwali Ahmed Saif<sup>1</sup> and Maged Alwan Noman<sup>1</sup>

<sup>1</sup>Professor Dr. of Pharmaceutics and Industrial Pharmacy, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.

<sup>2</sup>Professor Dr. of Medicinal Chemistry and Drug Design, Department of Medicinal Chemistry, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.

<sup>3</sup>Assistant Professor Dr. of Pharmacology and Toxicology, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.



\*Corresponding Author: Mahmoud Mahyoob Alburyhi

Professor Dr. of Pharmaceutics and Industrial Pharmacy, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.

DOI: <https://doi.org/10.5281/zenodo.20080560>

**How to cite this Article:** Mahmoud Mahyoob Alburyhi<sup>1\*</sup>, Tawfeek A.A. Yahya<sup>2</sup>, Mohammed A. AlKhawlani<sup>3</sup>, Abdalwali Ahmed Saif<sup>1</sup> and Maged Alwan Noman<sup>1</sup> (2026). Compatibility Studies of Azithromycin and Paracetamol Combination for the Development as Suppositories Novel Drug Delivery Systems. World Journal of Pharmaceutical and Life Sciences, 12(5), 309–334.

This work is licensed under Creative Commons Attribution 4.0 International license.



Article Received on 05/04/2026

Article Revised on 25/04/2026

Article Published on 01/05/2026

### ABSTRACT

The main objective of the present study was to the preformulation studies were performed to know the development of formulation and evaluation of Azithromycin Dihydrate and Paracetamol drugs in formulated suppositories Drug Delivery Systems. Azithromycin is classified as a biopharmaceutics classification system (BCS) Class-IV. Preformulation, formulation and evaluation of Azithromycin to avoid problems associated with conventional delivery system such as limited permeation, low dissolution and bioavailability and also to improve bioavailability and one of the most antibacterials agents. In the present study that the compatibility was assessed by, FTIR spectroscopy, and melting point apparatus, preformulation parameters. Results showed that physical mixtures of antibacterials and analgesic, antipyretic and various excipients as PEG4000, Witepsol were evaluated for preformulation studies parameters. It was concluded that the drug Azithromycin Dihydrate and Paracetamol was found to be compatible which were selected for the formulation development of the Azithromycin and Paracetamol drugs in formulated suppositories Novel Drug Delivery Systems. Formulation scientist from his experience and knowledge have to significantly in the preformulation study stage and is an important factor in the NDDS (Novel Drug Delivery Systems) product development process.

**KEYWORDS:** Azithromycin Dihydrate, Paracetamol, Compatibility, Suppositories, Preformulation, Formulation, Antibiotics, Analgesic and Antipyretic.

### INTRODUCTION

#### Background<sup>[1-24]</sup>

Azithromycin is a broad-spectrum macrolide antibiotic with a long half-life and a high degree of tissue penetration.<sup>[3]</sup> It was initially approved by the FDA in 1991. It is primarily used for the treatment of respiratory, enteric and genitourinary infections and may be used instead of other macrolides for some sexually transmitted and enteric infections. It is structurally related to

erythromycin. Azithromycin is a second-generation, semi-synthetic macrolide antibiotic belonging to the azalide subclass. It acts by binding to the 50S subunit of bacterial ribosomes, inhibiting protein synthesis by blocking peptide translocation during the elongation phase. This mechanism confers bacteriostatic activity against susceptible organisms, although bactericidal effects can occur at higher concentrations or against certain pathogens. The spectrum of activity of

azithromycin encompasses many clinically relevant pediatric pathogens, including respiratory tract pathogens (*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*), certain enteric pathogens, and atypical organisms. This broad spectrum makes azithromycin particularly valuable for empiric therapy in community-acquired infections. Pharmacokinetically, azithromycin demonstrates several advantageous properties for pediatric use. Following oral administration in children, it is rapidly absorbed, achieving peak plasma concentrations (C<sub>max</sub>) of 224-383 µg/L within approximately 2 hours, depending on age group and dosage regimen. However, its oral bioavailability is relatively low (approximately 38% in adults) due to first-pass metabolism.

A distinguishing pharmacokinetic feature of azithromycin is its extensive tissue distribution and intracellular accumulation. The drug achieves concentrations in infected tissues and cells that significantly exceed plasma levels, often by 10- to 100-fold. This distribution pattern, coupled with a long elimination half-life (32-64 hours in children), allows for once-daily dosing and short treatment courses, typically 3-5 days. In pediatric clinical practice, azithromycin is primarily used for respiratory tract infections (including community-acquired pneumonia, acute otitis media, and pharyngitis), skin and soft tissue infections, and certain sexually transmitted infections in adolescents. Standard pediatric dosing is 10 mg/kg on day one, followed by 5 mg/kg on days 2-5, or alternatively, a single 30 mg/kg dose in specific indications like acute otitis media.

Acetaminophen (paracetamol), also commonly known as *Tylenol*, is the most commonly taken analgesic worldwide and is recommended as first-line therapy in pain conditions by the World Health Organization (WHO). It is also used for its antipyretic effects, helping to reduce fever. This drug was initially approved by the U.S. FDA in 1951 and is available in a variety of forms including syrup form, regular tablets, effervescent tablets, injection, suppository, and other forms. Acetaminophen is often found combined with other drugs in more than 600 over the counter (OTC) allergy medications, cold medications, sleep medications, pain relievers, and other products. Confusion about dosing of this drug may be caused by the availability of different formulas, strengths, and dosage instructions for children of different ages. Due to the possibility of fatal overdose and liver failure associated with the incorrect use of acetaminophen, it is important to follow current and available national and manufacturer dosing guidelines while this drug is taken or prescribed. On September 22, 2025, the US FDA initiated a labeling change for acetaminophen products suggesting that the use of acetaminophen by pregnant women may be associated with an increased risk of neurological conditions such as autism and ADHD in children. While the FDA updated labeling to caution about potential risks, large studies,

national and international health authorities, and professional organizations - including the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the American College of Obstetricians and Gynecologists (ACOG) maintain that acetaminophen use in pregnancy remains a first-line therapeutic option when used at the lowest effective dose for the shortest required duration.

Paracetamol is a non-opioid analgesic and antipyretic with minimal anti-inflammatory properties. Its mechanism of action is not fully elucidated but is thought to involve inhibition of prostaglandin synthesis in the central nervous system and effects on descending serotonergic pathways. Unlike nonsteroidal anti-inflammatory drugs (NSAIDs), paracetamol has minimal peripheral effects on cyclooxygenase enzymes, explaining its weak anti-inflammatory activity and favorable gastrointestinal safety profile.

Pharmacokinetically, paracetamol demonstrates good oral bioavailability (approximately 60-89% in children), with peak plasma concentrations occurring within 30-60 minutes of oral administration. However, rectal absorption is generally slower and more variable, with bioavailability ranging from 24% to 98% depending on the formulation and individual factors. The elimination half-life of paracetamol in children ranges from 1-3 hours, necessitating multiple daily doses for sustained effect.

Paracetamol undergoes extensive hepatic metabolism, primarily via glucuronidation and sulfation, with a minor pathway involving cytochrome P450 enzymes (particularly CYP2E1) leading to the formation of a potentially toxic metabolite, N-acetyl-p-benzoquinoneimine (NAPQI). At therapeutic doses, this metabolite is efficiently detoxified by glutathione conjugation, but in overdose situations, glutathione stores may be depleted, leading to hepatotoxicity. In pediatric practice, paracetamol is widely used for fever management and pain control in various clinical scenarios, including infectious diseases. Standard pediatric dosing is 10-15 mg/kg every 4-6 hours, with a maximum of 4-5 doses per 24 hours. The drug's favorable safety profile at therapeutic doses makes it a first-line antipyretic in pediatric populations, though careful attention to proper dosing is essential to avoid toxicity.

#### **Rationale for Combination**

The combination of azithromycin and paracetamol addresses complementary aspects of bacterial infection management: pathogen eradication and symptom control. While there are no direct pharmacokinetic interactions reported between these agents that would preclude their co-administration, their combined use in a single formulation represents a novel approach that could potentially enhance treatment acceptability, compliance, and outcomes in pediatric populations. Recent research

has suggested potential synergistic effects between certain antibiotics, including azithromycin, and paracetamol, though this area requires further investigation. Even without direct antimicrobial synergy, the symptomatic relief provided by paracetamol may indirectly support antibiotic effectiveness by improving overall patient condition and potentially enhancing immune function through fever control.

#### Advanced Rectal Formulation Strategies

Recent advances in rectal drug delivery have focused on enhancing drug bioavailability, improving patient acceptability, and developing controlled-release systems. Several innovative approaches have emerged: Hollow-type suppositories: containing a central cavity filled with drug in solid, liquid, or semi-solid form. This design prevents direct contact between the drug and suppository base, potentially reducing incompatibilities and allowing for controlled release characteristics. Dimple-type suppositories: with one or more surface indentations where drugs are concentrated. This design aims to enhance drug release by creating a concentration gradient for passive diffusion across the rectal mucosa. Liquid suppositories: incorporating thermosensitive or mucoadhesive polymers (or both) that remain liquid at room temperature for easy administration but solidify or thicken at body temperature to enhance retention. These formulations offer the ease of administration associated with liquid forms while minimizing leakage issues. Self-emulsifying drug delivery systems (SEDDS): designed to form oil-in-water emulsions upon contact with rectal fluids, enhancing the solubility and absorption of poorly water-soluble drugs. This approach has shown promising results for improving the bioavailability of various drugs administered rectally. Ion composition-modified enemas: designed to optimize drug delivery either locally or systemically. Research has demonstrated that the osmolarity and electrolyte composition of the enema can significantly influence whether the drug acts locally in the colorectal tissue or is absorbed systemically.

#### Studies on Rectal Antibiotic Delivery in Pediatrics

Several studies have investigated the rectal administration of antibiotics in pediatric populations, though this approach remains less common than oral or parenteral routes. Early studies focused primarily on aminopenicillins, with variable results regarding bioavailability and clinical efficacy.

For rectal azithromycin specifically, limited research is available. One published study reported a measurable but low (3.2%) bioavailability for a basic azithromycin suppository formulation. However, more recent research has demonstrated that optimized formulations can significantly enhance rectal bioavailability.

A promising study by Kauss *et al.* (2013) developed and characterized a polyethylene glycol (PEG) solid solution suppository formulation of azithromycin for pediatric use. In animal models, this formulation achieved

approximately 43% bioavailability relative to intravenous administration, which compared favorably to the target of 38% (oral product bioavailability in humans). This suggests that with appropriate formulation strategies, the rectal bioavailability of azithromycin can approach that of oral administration.

Another study by Kauss *et al.* (2012) screened various azithromycin rectal formulations, including hydrogels, hard gelatin capsules, and PEG suppositories, comparing their *in vivo* bioavailability in rabbits. The PEG suppository demonstrated the highest bioavailability (approximately 28% relative to IV) and produced plasma concentrations potentially sufficient for therapeutic effect. However, the onset of action was somewhat delayed compared to other formulations, with peak plasma concentrations occurring approximately 1.67 hours after administration.

These findings suggest that with optimal formulation design, rectal administration of azithromycin can achieve clinically relevant bioavailability, potentially providing a viable alternative to oral administration in specific pediatric scenarios. However, the literature on rectal co-administration of azithromycin with other drugs, including paracetamol, remains sparse, highlighting a knowledge gap that the current research aims to address.

#### Studies on Combined Antibiotic-Antipyretic Formulations

The concept of combining antibiotics with antipyretics in a single dosage form represents a relatively novel approach in pharmaceutical development, with limited published studies specifically addressing this combination. Most clinical practice involves the separate administration of these drug classes, with antibiotics targeting the infectious pathogen and antipyretics/analgesics managing associated symptoms.

#### Rationale for Combined Formulations

Several theoretical advantages support the development of combined antibiotic-antipyretic formulations: Simplified administration: Combination products reduce the number of medications to be administered, potentially improving adherence, especially in pediatric populations where medication administration can be challenging. Coordinated symptom management and antimicrobial therapy: Simultaneous delivery ensures that fever and pain are addressed concurrently with the initiation of antimicrobial activity. Potential pharmacological interactions: Some studies suggest that certain antipyretics may influence immune function or antibiotic efficacy, though the clinical significance of these effects requires further investigation. Practical considerations in resource-limited settings: In areas with limited healthcare access, simplified regimens that address both infection and symptoms could be particularly valuable.

**Pharmaceutical Research Paths**<sup>[25-92]</sup>

Pharmaceutical research is characterized by having both a natural source and synthetic source for primary active raw materials and excipients, each source is mainly prepared to the effectiveness and safety of the drug.

The Pharmaceutical Research Paths include: Pharmacognosy deals with natural sources of drug, Pharmaceutical Chemistry specializes in synthetic sources of drug, Pharmaceutics specializes in designing of pharmaceutical dosage forms and drug delivery systems from natural and synthetic sources of active pharmaceutical ingredients and excipients that help in developing dosage forms and drug delivery systems.

The Pharmaceutical Research Paths link steps are manufacturing and development of drug according to the standard parameters evaluation such as physiochemical properties, preformulation, formulation, evaluation, drug stability, Pharmaceutical analysis, pre-clinical, post-clinical stages, pre-marketing, post-marketing, Pharmacovigilance, Pharmacoeconomics, Pharmacy Management, Pharmacology, Toxicology, Therapeutics, Pharmaceutical Care, Health Care, Advanced Industrial Pharmacy, Biopharmaceutics and Pharmacokinetics, Advanced Clinical Pharmacokinetics, Pharmaceuticals Cosmetics, Pharmaceutical Biotechnology, Drug Design, Pharmacy Law and Ethics, Pharmacogenomics, Good Manufacturing Practice, and Good Pharmacy Practice etc.

All of these Pharmaceutical Research Paths are interconnected, and whenever the link between them is made in a scientific relationship and the goal of pharmaceutical care is achieved gradually according to plan of a scientific pharmaceutical research path.

Pharmaceutical Research Paths are the scientific methods through which the scientific relationship between the pharmaceutical team, research, supervisor or specialist researcher, the scientific research materials, equipment's, scientific institution, pharmaceutical companies, reference standards, and the goals of pharmaceutical research improve and development of community services of pharmaceutical care and health care.

Pharmaceutical Scientists are considering natural sources and medicinal herbs in the pharmaceutical industry an important part of drug development because natural sources of drugs have properties that are greater than industrial sources of drugs in NDDS. And the pharmaceutical industry strategies depend on the development of different pharmaceutical dosage forms and recent novel drug delivery systems. Using medicinal herbs and natural sources as important goals of drug development. It is part of the art of innovation in drug development with different of novel drug delivery systems and pharmaceutical care for patients and society, it's the basic of development of the new pharmaceutical

industry by developing different novel drug delivery systems from different sources.

**Importance of Drug-Excipient Compatibility**<sup>[93-165]</sup>

Studies of active pharmaceutical ingredient (API)-excipient compatibility represent an important study in the preformulation stage of the development of new dosage forms, stability of the dosage form can be maximized, any physical or chemical interaction between API, and excipient can affect bioavailability and stability of drug, it helps to avoid the surprise problem, by performing drug excipient compatibility studies (DECS) we can know the possible reaction before formulating final dosage form, DECS data is essential for IND (investigational new drug) submission, and now, USFDA has made it compulsory to submit DECS data for any new coming formulation before its approval.

The potential physical and chemical interactions between an API, and the excipients can affect the chemical nature, the stability and bioavailability of the former and, consequently, its therapeutic efficacy and safety, solid dosage forms are generally less stable than their API components and despite the importance of API-excipient compatibility testing, there is no universally accepted protocol to assess such interactions.

Pharmaceutical Excipients: Excipients are additive substances used to improve the bulkiness, disintegration, dissolution rate, and bioavailability of a formulation etc. Different dosage forms like powders, granules, capsules, tablets, oral liquids, injectable products, implants, eye products, nasal products, inhalers, topical creams, ointments, gels, transdermal patches and suppositories etc, contains different types of excipients. To make it acceptable and compatible various pharmaceutical excipients are added in pharmaceutical dosage form for their direct therapeutic action, manufacturing process, to protect, support or enhance stability, for bioavailability or patient compliance. These must be physiologically and chemically stable, must not have any incompatibility with the API, and must meet the standards of regulatory requirements.

**Evaluation of Drug-Excipient Compatibility**

The compatibility study of API and excipients is important to predict the stability of the API, in the final pharmaceutical product. It's the first time that API was compatible with excipients promoted physical and chemical compatibility studies was achieved by thermal and non-thermal methods. As a part of preformulation study, a compatibility study of API with the other excipients was carried out using physical blends in analytical techniques for the evaluation of drug-excipient interactions. The most commonly used pharmaceutical analytical techniques include, thermal techniques such as Differential Scanning Calorimetry (DSC), Thermogravimetric Analysis (TGA), Isothermal Microcalorimetry (IMC) and Hot stage microscopy (HSM) etc, and non-thermal techniques such as UV-

Visible Spectrophotometric (UV), Infrared, Near-Infrared and Raman Spectroscopy (FT-IR), (NIR), Powder X-Ray Diffraction (PXRD), Solid-State Nuclear Magnetic Resonance Spectroscopy (ssNMR), Microscopic techniques: Scanning Electron Microscopy (SEM), Chromatographic techniques: Thin Layer Chromatography (TLC), and High-Performance Liquid Chromatography (HPLC) etc.

**Preformulation Parameters:** According to dosage form of API, mainly solid state, particle size, shape, pKa, pH determination, common ion effect, temperature, partition coefficient, solubility studies, dissolution rate, melting point, powder flow properties, crystallinity, polymorphism, hygroscopicity, stability study and drug-excipient compatibility etc. While other dosage forms according to important of preformulation parameters used in study before start in development of formulation.

Drug-excipient compatibility and formulation stability is not depended on API only but also its affected by excipient. Excipient play important role in dosage form but side by side it also increases compatibility problem so proper selection of excipient is very important in development of formulation. Incompatibility can be result mainly in any of following changes: Changes in organoleptic properties, changes in dissolution performance, decrease in potency, and increase in degradation rate etc.

Drug excipient physicochemical characterization is a systematic approach towards design of therapeutically active and stable dosage forms. The rapid advancements in novel drug delivery systems development have led to an interest by formulation scientists in the role and functionality of the excipients.

In the present study, it was proposed to Azithromycin Dihydrate and Paracetamol (Acetaminophen) -excipient compatibility studies of the safety, efficacy, quality and stability of a formulation are major concepts of any APIs development process. In API development process, a

detailed characterization of the API and other formulation components is usually carried out during the preformulation stage., with commonly different excipients using for formulation development of Suppositories Novel Drug Delivery Systems.

## MATERIALS AND METHODS

### MATERIALS

**Azithromycin Dihydrate:** Active Pharmaceutical Ingredient (API), Zhejiang Guobang Pharmaceutical Co. Ltd., China. **Paracetamol (Acetaminophen):** Active Pharmaceutical Ingredient (API), Anhui Pharmaceutical Co. Ltd., China. **Witepsol H35 and Witepsol W76:** Lipophilic suppository bases, IOI Oleochemical, Germany. **Sodium Citrate:** Buffer agent/Stabilizer, Magnesia GMBH, Germany. **Sodium Lauryl Sulfate (SLS):** Anionic surfactant/Solubilizing agent, Vinamax Organics PVT. Ltd., India. **Sodium Starch Glycolate:** Super-disintegrant, DFE Pharma Excipient GMPH, Germany. **Polyethylene Glycol (PEG) 400:** Hydrophilic base component/Solvent, Magnesia GMBH, Germany. **Polyethylene Glycol (PEG) 6000:** Hydrophilic base component, Magnesia GMBH, Germany. **Tween 80 (Polysorbate 80):** Non-ionic surfactant, Magnesia GMBH, Germany. **0.1N Hydrochloric Acid (HCl).** **Potassium Bromide (KBr).** **Distilled Water (DW).** **Phosphate Buffer.**

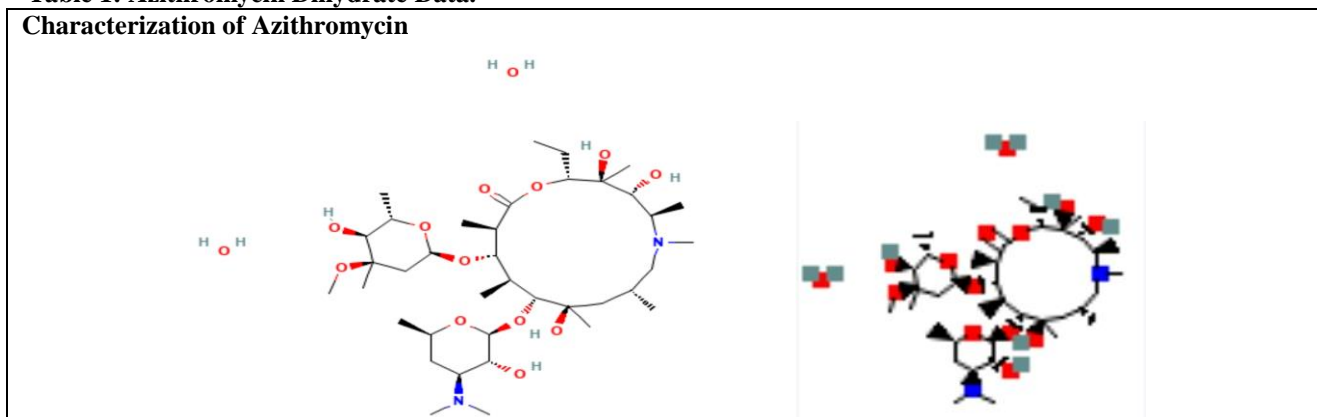
### Equipment's

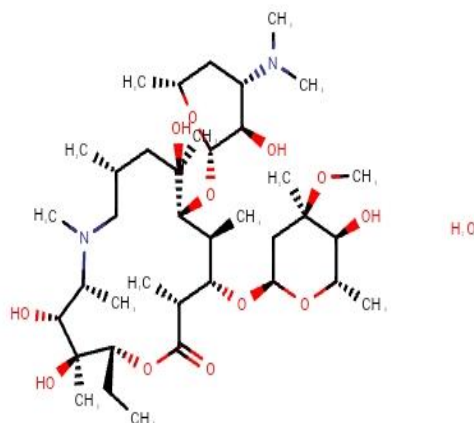
**UV-Visible Spectrophotometer:** Model N630, Jasco, Japan. **Infrared (IR) Spectrometer:** Model Nicolet IS10, Thermo Scientific, USA. **Melting Point Tester:** Model SMP30, Stuart (Bibby Scientific), UK. **High-Performance Liquid Chromatography (HPLC) System:** Model LC-2050C 3D, Shimadzu, Japan. **pH Meter:** Model 3520, Jenway, Hong Kong. **Analytical Balance:** Model Sartorius, Mettler, USA. **Hot Plate/Heater:** Model GMR 160, Geremi, UK. **Oven:** Model GPS.100 CLAD250 DIG, Widnes Cheshire, England. **Refrigerator:** Model RT6000K, Samsung, South Korea. **Disintegration Thermionic:** Model DSP-3, Compbell Electronics, India. **Suppository Molds.**

## Preformulation Studies

### Evaluation of Drug-Excipient Compatibility Studies Methods<sup>[21-24,150-221]</sup>

**Table 1: Azithromycin Dihydrate Data.**

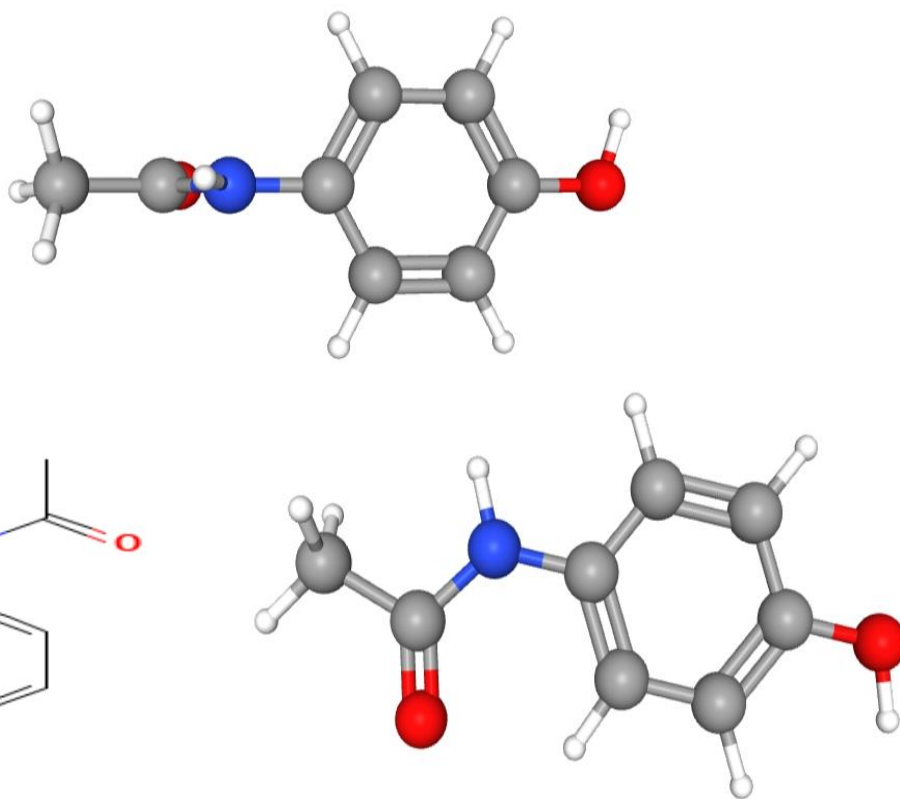




### Azithromycin Dihydrate Structure and 3D Conformer.

<b>Chemical Structure</b>	(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-11-[(2S,3R,4S,6R)-4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy-2-ethyl-3,4,10-trihydroxy-13-[(2R,4R,5S,6S)-5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl]oxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-azacyclopentadecan-15-one.	<b>Appearance</b>	White crystalline powder.
<b>Molecular Formula</b>	<b>MF:</b> C <sub>38</sub> H <sub>76</sub> N <sub>2</sub> O <sub>14</sub>	<b>Drug Solubility</b>	<b>Water Solubility:</b> Is characterized as a water-insoluble. Soluble in ethanol and DMSO. <b>Melting Point</b> Amorphous solid, mp: 113°C.-115°C. Mp:122- 126°C
<b>Molecular Weight</b>	MW: 785.026g/mol	<b>BCS</b>	Class-IV.
<b>Drug Action and Use</b>	<p><b>An antibiotic medication used to treat a variety of infections caused by bacteria.</b></p> <p><b>Azithromycin</b> is a macrolide antibiotic used to treat a variety of bacterial infections. zithromycin [9-deoxo-9a-aza-9a-methyl-9a-homoerythromycin] is a part of the <i>azalide</i> subclass of macrolides, and contains a 15-membered ring, with a methyl-substituted nitrogen instead of a carbonyl group at the 9a position on the aglycone ring, which allows for the prevention of its metabolism. This differentiates azithromycin from other types of macrolides.</p> <p>Azithromycin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria in order to prevent the development antimicrobial resistance and maintain the efficacy of azithromycin.</p> <p>Azithromycin is indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of the microorganisms listed in the specific conditions below.</p> <p><b>Adults:</b> Acute bacterial exacerbations of chronic obstructive pulmonary disease due to <i>Haemophilus influenzae</i>, <i>Moraxella catarrhalis</i> or <i>Streptococcus pneumoniae</i> Acute bacterial sinusitis due to <i>Haemophilus influenzae</i>, <i>Moraxella catarrhalis</i> or <i>Streptococcus pneumoniae</i> Community-acquired pneumonia due to <i>Chlamydophila pneumoniae</i>, <i>Haemophilus influenzae</i>, <i>Mycoplasma pneumoniae</i> or <i>Streptococcus pneumoniae</i> in patients appropriate for oral therapy Pharyngitis/tonsillitis caused by <i>Streptococcus pyogenes</i> as an alternative to first-line therapy in individuals who cannot use first-line therapy. Uncomplicated skin and skin structure infections due to <i>Staphylococcus aureus</i>, <i>Streptococcus pyogenes</i>, or <i>Streptococcus agalactiae</i>. Abscesses usually require surgical drainage. Urethritis and cervicitis due to <i>Chlamydia trachomatis</i> or <i>Neisseria gonorrhoeae</i>.</p> <p><b>Pediatric Patients</b> Acute otitis media caused by <i>Haemophilus influenzae</i>, <i>Moraxella catarrhalis</i> or <i>Streptococcus pneumoniae</i>, Community-acquired pneumonia due to <i>Chlamydophila pneumoniae</i>, <i>Haemophilus influenzae</i>, <i>Mycoplasma pneumoniae</i> or <i>Streptococcus pneumoniae</i> in patients appropriate for oral</p>		

	<p>therapy. Pharyngitis/tonsillitis caused by <i>Streptococcus pyogenes</i> as an alternative to first-line therapy in individuals who cannot use first-line therapy.</p> <p><b>Pharmacodynamics</b> Macrolides stop bacterial growth by inhibiting protein synthesis and translation, treating bacterial infections<sup>4</sup>. Azithromycin has additional immunomodulatory effects and has been used in chronic respiratory inflammatory diseases for this purpose<sup>3</sup>.</p> <p><b>Mechanism of action</b> In order to replicate, bacteria require a specific process of protein synthesis, enabled by ribosomal proteins. Azithromycin binds to the 23S rRNA of the bacterial 50S ribosomal subunit. It stops bacterial protein synthesis by inhibiting the transpeptidation/translocation step of protein synthesis and by inhibiting the assembly of the 50S ribosomal subunit. This results in the control of various bacterial infections. The strong affinity of macrolides, including azithromycin, for bacterial ribosomes, is consistent with their broad-spectrum antibacterial activities. Azithromycin is highly stable at a low pH, giving it a longer serum half-life and increasing its concentrations in tissues compared to erythromycin.</p>		
<b>Azithromycin Pharmacokinetics</b>			
<b>Drug Absorption</b>	<p>Bioavailability of azithromycin is 37% following oral administration. Absorption is not affected by food. Macrolide absorption in the intestines is believed to be mediated by P-glycoprotein (ABCB1) efflux transporters, which are known to be encoded by the <i>ABCB1</i> gene.</p>	<b>Drug Distribution</b>	<p><b>Volume Distribution</b> After oral administration, azithromycin is widely distributed in tissues with an apparent steady-state volume of distribution of 31.1 L/kg. Significantly greater azithromycin concentrations have been measured in the tissues rather than in plasma or serum. The lung, tonsils and prostate are organs have shown a particularly high rate of azithromycin uptake. This drug is concentrated within macrophages and polymorphonucleocytes, allowing for effective activity against <i>Chlamydia trachomatis</i>. In addition, azithromycin is found to be concentrated in phagocytes and fibroblasts, shown by in vitro incubation techniques. In vivo studies demonstrate that concentration in phagocytes may contribute to azithromycin distribution to inflamed tissues.</p> <p><b>Protein Binding:</b> The serum protein binding of azithromycin varies in humans, decreasing from 51% at 0.02 µg/mL to 7% at 2 µg/mL.</p>
<b>Drug Metabolism</b>	<p>In vitro and in vivo studies to assess the metabolism of azithromycin have not been performed however, this drug is eliminated by the liver.</p>	<b>Drug Excretion</b>	<p><b>Route of elimination:</b> Biliary excretion of azithromycin, primarily as unchanged drug, is a major route of elimination. Over a 1 week period, approximately 6% of the administered dose is found as unchanged drug in urine.</p> <p><b>Clearance:</b> Mean apparent plasma cl=630 mL/min (following single 500 mg oral and i.v. dose).</p>
<b>The Elimination Half-Life (T<sub>1/2</sub>)</b>	<p>Terminal elimination half-life: 68 hours.</p>	<b>Availability</b>	<p>Powder for Suspension, Injection, Tablet, film coated, Tablet, coated.</p>

**Table 2: Paracetamol (Acetaminophen) Data.****Characterization of Paracetamol (Acetaminophen)****Paracetamol (Acetaminophen) Structure and 3D Conformer.**

<b>Chemical Structure</b>	4-Acetamidophenol; 103-90-2; N-(4-Hydroxyphenyl)acetamide	<b>Appearance</b>	A <b>white crystalline</b> or a crystalline powder.
<b>Molecular Formula</b>	<b>MF:</b> C <sub>8</sub> H <sub>9</sub> NO <sub>2</sub>	<b>Drug Solubility</b>	<b>Water Solubility:</b> Is sparingly soluble in cold water but shows much higher solubility in polar organic solvents like ethanol and acetone. <b>Melting Point:</b> 168°C-172°C.
<b>Molecular Weight</b>	MW: 151.16 g/mol	<b>BCS</b>	Class-III.
<b>Drug Action and Use</b>	<p><b>A medication used to reduce fever and treat pain.</b></p> <p><b>Acetaminophen</b> is an analgesic drug used alone or in combination with opioids for pain management, and as an antipyretic agent.</p> <p>In general, acetaminophen is used for the treatment of mild to moderate pain and reduction of fever. It is available over the counter in various forms, the most common being oral forms.</p> <p>Acetaminophen <i>injection</i> is indicated for the management of mild to moderate pain, the management of moderate to severe pain with adjunctive opioid analgesics, and the reduction of fever.</p> <p>Because of its low risk of causing allergic reactions, this drug can be administered in patients who are intolerant to salicylates and those with allergic tendencies, including bronchial asthmatics. Specific dosing guidelines should be followed when administering acetaminophen to children.</p> <p><b>Mechanism of action:</b> One theory is that acetaminophen increases the pain threshold by inhibiting two isoforms of cyclo-oxygenase, COX-1 and COX-2, which are involved in prostaglandin (PG) synthesis. Prostaglandins are responsible for eliciting pain sensations. Acetaminophen does not inhibit cyclooxygenase in peripheral tissues and, therefore, has no peripheral anti-inflammatory effects. Though acetylsalicylic acid (aspirin) is an irreversible inhibitor of COX and directly blocks the active site of this enzyme, studies have shown that acetaminophen (paracetamol) blocks COX indirectly. Studies also suggest that acetaminophen selectively blocks a variant type of the COX enzyme that is unique from the known variants COX-1 and COX-2. This enzyme has been referred to as <i>COX-3</i>. The</p>		

	<p>antipyretic actions of acetaminophen are likely attributed to direct action on heat-regulating centers in the brain, resulting in peripheral vasodilation, sweating, and loss of body heat. The exact mechanism of action of this drug is not fully understood at this time, but future research may contribute to deeper knowledge.</p> <p>Although further investigation is warranted, the active metabolite of acetaminophen (AM404) was shown to interact with several molecular targets, including the Ca<sub>v</sub>3.2 calcium channel, the cannabinoid CB1 receptors, TRPV1 receptors, and Na<sub>v</sub>1.8 and Na<sub>v</sub>1.7 channels.</p>		
<b>Paracetamol Pharmacokinetics</b>			
<b>Drug Absorption</b>	<p>Acetaminophen has 88% oral bioavailability and reaches its highest plasma concentration 90 minutes after ingestion. Peak blood levels of free acetaminophen are not reached until 3 hours after rectal administration of the suppository form of acetaminophen and the peak blood concentration is approximately 50% of the observed concentration after the ingestion of an equivalent oral dose (10-20 mcg/mL). The percentage of a systemically absorbed rectal dose of acetaminophen is inconsistent, demonstrated by major differences in the bioavailability of acetaminophen after a dose administered rectally. Higher rectal doses or an increased frequency of administration</p>	<b>Drug Distribution</b>	<p><b>Volume Disrtbution:</b> Volume of distribution is about 0.9L/kg. 10 to 20% of the drug is bound to red blood cells. Acetaminophen appears to be widely distributed throughout most body tissues except in fat.</p> <p><b>Protien Binding:</b> The binding of acetaminophen to plasma proteins is low (ranging from 10% to 25%), when given at therapeutic doses.</p>

	may be used to attain blood concentrations of acetaminophen similar to those attained after oral acetaminophen administration.		
<b>Drug Metabolism</b>	<p>Acetaminophen is the major metabolite of <i>phenacetin</i> and <i>acetanilid</i>. Acetaminophen is mainly metabolized in the liver by first-order kinetics and its metabolism of comprised of 3 pathways: conjugation with glucuronide, conjugation with sulfate, and oxidation through the cytochrome P450 enzyme pathway, mainly CYP2E1, to produce a reactive metabolite (N-acetyl-p-benzoquinone imine or NAPQI). At normal therapeutic doses, NAPQI undergoes fast conjugation with glutathione and is subsequently metabolized to produce both cysteine and mercapturic acid conjugates. High doses of acetaminophen (overdoses) can lead to hepatic</p>	<b>Drug Excretion</b>	<p><b>Route of elimination:</b> Acetaminophen metabolites are mainly excreted in the urine. Less than 5% is excreted in the urine as free (unconjugated) acetaminophen and at least 90% of the administered dose is excreted within 24 hours.</p> <p><b>Clearance:</b> Adults: 0.27 L/h/kg following a 15 mg/kg intravenous (IV) dose. Children: 0.34 L/h/kg following a 15 mg/kg intravenous (IV) dose).</p>

	<p>necrosis due to the depletion of glutathione and of binding of high levels of reactive metabolite (NAPQI) to important parts of liver cells. The above mentioned damage to the liver can be prevented by the early administration of sulfhydryl compounds, for example, methionine and N-acetylcysteine.</p> <p><b>Overdose and Liver Toxicity:</b> Acetaminophen overdose may be manifested by renal tubular necrosis, hypoglycemic coma, and thrombocytopenia. Sometimes, liver necrosis can occur as well as liver failure. Death and the requirement of a liver transplant may also occur. Metabolism by the CYP2E1 pathway releases a toxic acetaminophen metabolite known as <i>N-acetyl-p-benzoquinoneimine</i> (NAPQI). The toxic effects caused by this drug are attributed to NAPQI, not acetaminophen alone.</p>		
--	--	--	--

<b>The Elimination Half-Life (T<sub>1/2</sub>)</b>	The half-life for adults is 2.5 h after an intravenous dose of 15 mg/kg. After an overdose, the half-life can range from 4 to 8 hours depending on the severity of injury to the liver, as it heavily metabolizes acetaminophen.	<b>Availability</b>	Liquid, Tablet, Injection, solution, Tablet, chewable, Tablet, film coated, extended release, Suppository.
--	--	---------------------	--

**Table 3: Pharmaceutical Excipients Data.**

Nonproprietary Name	Chemical Name	Functional Category	Incompatibilities
<b>Sodium Lauryl Sulfate</b>	Dodecyl alcohol hydrogen sulfate, sodium salt, dodecyl sodium sulfate, dodecyl sulfate sodium salt, Efan 240. C <sub>12</sub> H <sub>25</sub> NaO <sub>4</sub> S	Anionic surfactant; detergent; emulsifying agent; skin penetrant; tablet and capsule lubricant; wetting agent.	incompatible with salts of polyvalent metal ions, such as aluminum, lead, tin or zinc
<b>Tween 80</b>	Monolaurates, polyoxyethylene sorbitan, polysorbate	Emulsifying agent for the preparation of stable oil-in-water emulsions.	Incompatible with alkalis, heavy metal salts, phenols, tannic acid.
<b>Sodium Starch Glycolate</b>	Sodium carboxymethyl starch	Tablet and capsule disintegrant.	Incompatible with ascorbic acid.
<b>Polyethylene Glycol (PEG)</b>	BP: Macrogols JP: Macrogol 400 Macrogol 1500 Macrogol 4000 Macrogol 6000 Macrogol 20000 PhEur: Macrogola USPNF: Polyethylene glycol	Ointment base; plasticizer; solvent; suppository base; tablet and capsule lubricant.	The chemical reactivity of polyethylene glycols is mainly confined to the two terminal hydroxyl groups, which can be either esterified or etherified. However, all grades can exhibit some oxidizing activity owing to the presence of peroxide impurities and secondary products formed by autoxidation. Liquid and solid polyethylene glycol grades may be incompatible with some coloring agents. The antibacterial activity of certain antibiotics is reduced in polyethylene glycol bases, particularly that of penicillin and bacitracin. The preservative efficacy of the parabens may also be impaired owing to binding

			with polyethylene glycols. Physical effects caused by polyethylene glycol bases include softening and liquefaction in mixtures with phenol, tannic acid, and salicylic acid. Discoloration of sulfonamides and dithranol can also occur and sorbitol may be precipitated from mixtures. Plastics, such as polyethylene, phenolformaldehyde, polyvinyl chloride, and cellulose-ester membranes (in filters) may be softened or dissolved by polyethylene glycols. Migration of polyethylene glycol can occur from tablet film coatings, leading to interaction with core components
<b>Witepsol</b>	BP: Hard fat PhEur: Adeps solidus USPNF: Hard fat	Suppository base. The primary application of hard fat suppository bases, or semisynthetic glycerides, is as a vehicle for the rectal or vaginal administration of a variety of drugs, either to exert local effects or to achieve systemic absorption. Selection of a suppository base cannot usually be made in the absence of knowledge of the physicochemical properties and intrinsic thermodynamic activity of the drug substance. Other drug-related factors that can affect release and absorption and which must therefore be considered are the particle size distribution of insoluble solids, the oil : water partition coefficient, and the dissociation constant. The displacement value should also be known, as well as the ratio of drug to base. Properties of the suppository base that may or may not be modified by the drug, or that can influence drug release, are the melting characteristics, chemical reactivity, and rheology. The presence of additives in the base can also affect performance.	Incompatibilities with suppository bases are not now extensively reported in the literature. The occurrence of a chemical reaction between a hard fat suppository base and a drug is relatively rare, but any potential for such a reaction may be indicated by the magnitude of the hydroxyl value of the base.

According to **Azithromycin**, **Paracetamol** and excipients data as shown in Tables 1,2 and 3, it was selected that the different excipients to preformulation study with **Azithromycin and Paracetamol** in the present study.

#### **Suppository Formulations Preformulation Studies**

Preformulation studies are initiated to define the physical and chemical properties of the agent. The key goals of

preformulation studies are to ensure the delivery of drug product with acceptable stability, bioavailability, and manufacturability.

#### **Determination of the Solubility**

The approximate solubility of each API was determined in distilled water (DW), 0.1N hydrochloric acid (HCl), and phosphate buffer (pH not specified). A known excess amount of API (100 mg) was added to measured volumes of each solvent, agitated, and observed for

dissolution. Azithromycin Dihydrate: Found to be practically insoluble in DW (>100 mg requires >10,000 mL), soluble in 0.1N HCl (approx. 3.33 mg/mL, based on 100 mg in 30 mL), and slightly soluble in phosphate buffer (approx. 0.1 mg/mL, based on 100 mg in 1000 mL). Paracetamol: Found to be sparingly soluble in DW (approx. 1.25 mg/mL, based on 100 mg in 80 mL), 0.1N HCl (approx. 1.11 mg/mL, based on 100 mg in 90 mL), and phosphate buffer (approx. 1.25 mg/mL, based on 100 mg in 80 mL).

#### Determination of the Melting Point

The melting point of Azithromycin Dihydrate and the melting range of Paracetamol were determined using a capillary melting point apparatus (Stuart, Model SMP30). A small amount of each API powder was packed into a capillary tube and heated at a controlled rate.

#### UV-Visible (UV-Vis) Spectroscopy

Azithromycin Dihydrate: A solution was prepared by dissolving the API in 0.1N HCl (concentration specified as 5 mg/mL in the source document, although this seems high and might be a typo for 5 µg/mL). The spectrum was recorded using a UV-Vis spectrophotometer (Jasco, Model N630) against a 0.1N HCl blank.

Paracetamol: A solution was prepared by dissolving the API in DW (concentration specified as 0.01 mg/mL or 10µg/mL). The spectrum was recorded using the same instrument against a DW blank.

#### Infrared (IR) Spectroscopy

IR spectroscopy was employed for structural confirmation. A small amount of each API was intimately mixed with potassium bromide (KBr) powder (approximately 1:10 API:KBr ratio). The mixture was compressed into a transparent disc using a hydraulic press. The IR spectrum of each disc was obtained using an IR spectrophotometer (Thermo Scientific, Nicolet IS10) over a suitable wavenumber range (e.g., 4000-400 cm<sup>-1</sup>).

#### Drug-Excipient Compatibility Studies

A physical mixture including **Azithromycin** and Paracetamol was created in a 1:1 ratio, and it was

subjected to analytical techniques such as FTIR spectroscopy. FTIR, of both pure drug and physical mixture were obtained, and the spectra of the both drug and mixture of excipient with drug were compared to study for any incompatibilities.

#### Preparation of IR Samples

The sample was determined by the disc method. Triturate 5mg of the substance to be examined with 300-400 mg of finely powdered and dried potassium bromide R or potassium chloride R. Each excipient was mix with **Azithromycin** and Paracetamol equally then of potassium bromide is added to the mixture. Carefully grind the mixture, spread it uniformly in a suitable die, and submit it to a pressure of about 800 MPa (8 t·cm<sup>-2</sup>). Then the tablets were inserted to the device and the Infrared spectra was recorded at mild-infrared light in wavenumber range of 4000 cm<sup>-1</sup> to 400 cm<sup>-1</sup>. After that the spectra were compared with the reference.

#### Infrared Spectral Study of Samples in Room Condition

Compatibility studies were performed by preparing blend of different excipients with **Azithromycin** and Paracetamol in room condition.

### RESULTS AND DISCUSSION

#### Preformulation Studies

##### Solubility Study

Azithromycin Dihydrate exhibited solubility characteristics consistent with literature, being practically insoluble in distilled water (DW), soluble in 0.1N HCl (approximately 3.33 mg/mL based on 100 mg in 30 mL), and slightly soluble in phosphate buffer (approximately 0.1 mg/mL based on 100 mg in 1000 mL). Paracetamol was found to be sparingly soluble across the tested media: DW (approx. 1.25 mg/mL), 0.1N HCl (approx. 1.11 mg/mL), and phosphate buffer (approx. 1.25 mg/mL). These solubility profiles are crucial for understanding potential dissolution behavior and informing formulation strategies. As shown in Table 4.

**Table 4: Solubility Results of APIs in Different Media.**

Medium	Solubility of Azithromycin	Solubility of Paracetamol
Distilled Water	Practically insoluble	Sparingly soluble
(0.1N HCl)	Soluble	Sparingly soluble
Phosphate buffer	Slightly soluble	Sparingly soluble

#### Melting Point Determination

The melting point observed for Azithromycin Dihydrate was 126°C. Paracetamol exhibited a melting range of 168-172°C. These values align with typical reported ranges for these APIs and confirm their thermal identity. As shown in Tables 5 and 6.

Melting point of pure **Azithromycin** was determined by open capillary method. The capillary tube was closed at one end by fusion and was filled with **Azithromycin** by repeated tapings. The capillary tube was placed in a digital melting point apparatus. The instrument was set to automatically increase the temperature of the heating bath. The rise in temperature was viewed through screen.

The temperature at which the drug started melting was recorded. The melting point range of **Azithromycin** was identical to reference melting point stated in MP (122-126°C). The sample started to melt at 122°C, and turned into liquid at 126°C, indicating that the sample used is pure. That reading has stated in melting point tester.as shown in Table 5.

Melting point of pure Paracetamol was determined by open capillary method. The capillary tube was closed at one end by fusion and was filled with Paracetamol by

repeated tapings. The capillary tube was placed in a digital melting point apparatus. The instrument was set to automatically increase the temperature of the heating bath. The rise in temperature was viewed through screen. The temperature at which the drug started melting was recorded. The melting point range of Paracetamol was identical to reference melting point stated in MP (168-172°C). The sample started to melt at 168°C, and turned into liquid at 172°C, indicating that the sample used is pure. That reading has stated in melting point tester.as shown in Table 6.

**Table 5: Results of Melting Point of Azithromycin.**

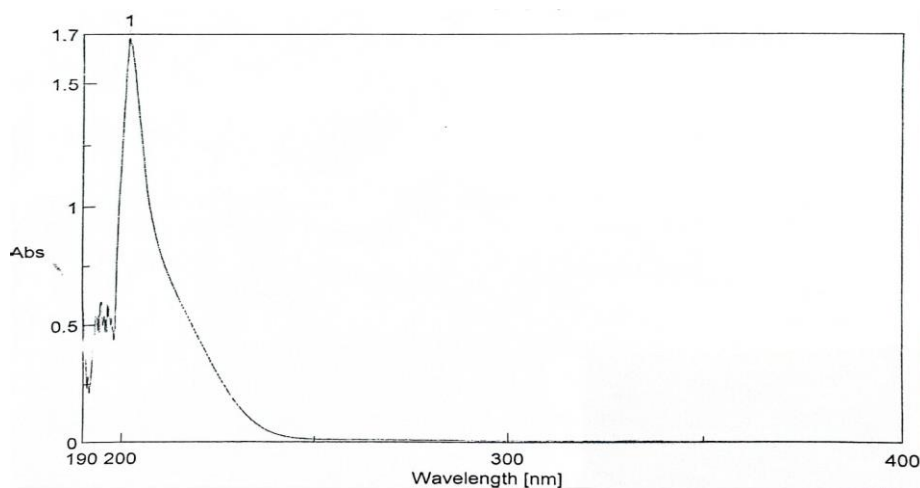
Test	Temp Rang Analyzed (Melting )	Results
Test I Azithromycin	(168-172°C)	172°C
Test II Azithromycin	(168-172°C)	172°C

**Table 6: Results of Melting Point of Paracetamol.**

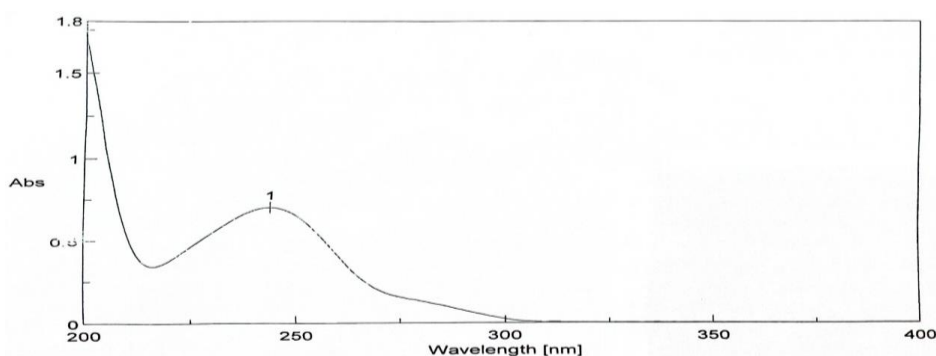
Test	Temp Rang Analyzed (Melting)	Results
Test I Paracetamol	(168-172°C)	172°C
Test II Paracetamol	(168-172°C)	172°C

### Spectroscopic Identification

UV-Vis spectroscopic analysis was performed. Azithromycin in 0.1N HCl and Paracetamol in DW yielded characteristic spectra confirming their identity. As shown in Figures 1 and 2.



**Fig. 1: UV-Visible Spectrum of Azithromycin.**



**Fig. 2: UV-Visible Spectrum of Paracetamol.**

### Characterization of Azithromycin by FTIR

FTIR spectrum studies indicated that major functional groups present in **Azithromycin** show characteristic peaks in IR spectrum. Figure (3) show peaks observed at different wave numbers and the functional group associated with these peaks for drug. The major peaks are identical to functional group of **Azithromycin**. Hence, it was confirmed that there was compatibility. As shown in Figure 4.

### Characterization of Paracetamol by FTIR

FTIR spectrum studies indicated that major functional groups present in **Paracetamol** show characteristic peaks in IR spectrum. Figure (5) show peaks observed at different wave numbers and the functional group associated with these peaks for drug. The major peaks are identical to functional group of **Paracetamol**. Hence, it was confirmed that there was compatibility. As shown in Figure 6.

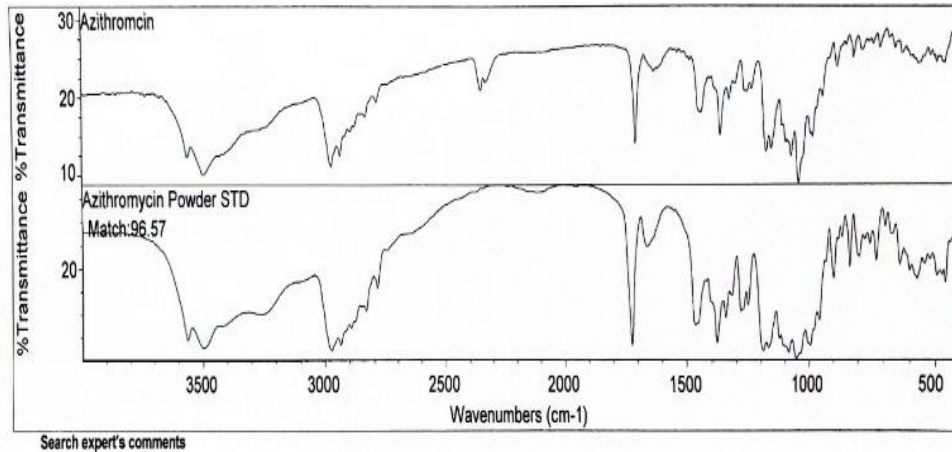


Fig. 3: FTIR Spectrum of Azithromycin STD.

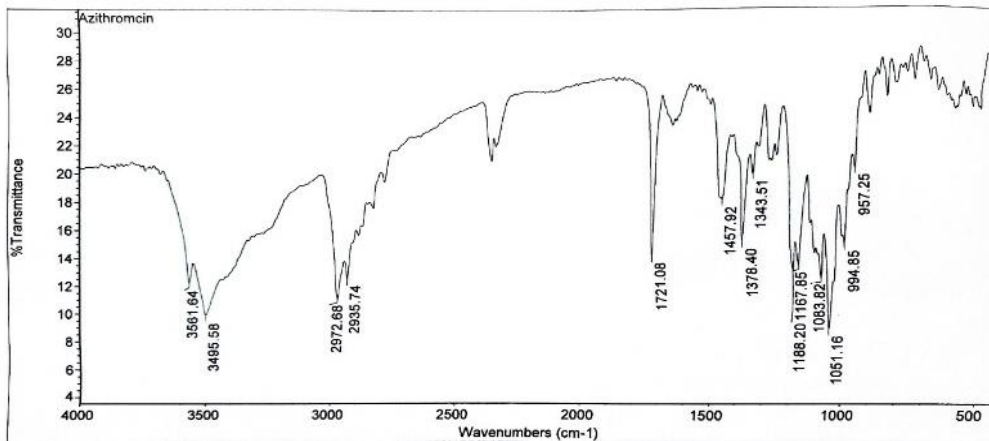


Fig. 4: FTIR Spectrum of Pure Azithromycin.

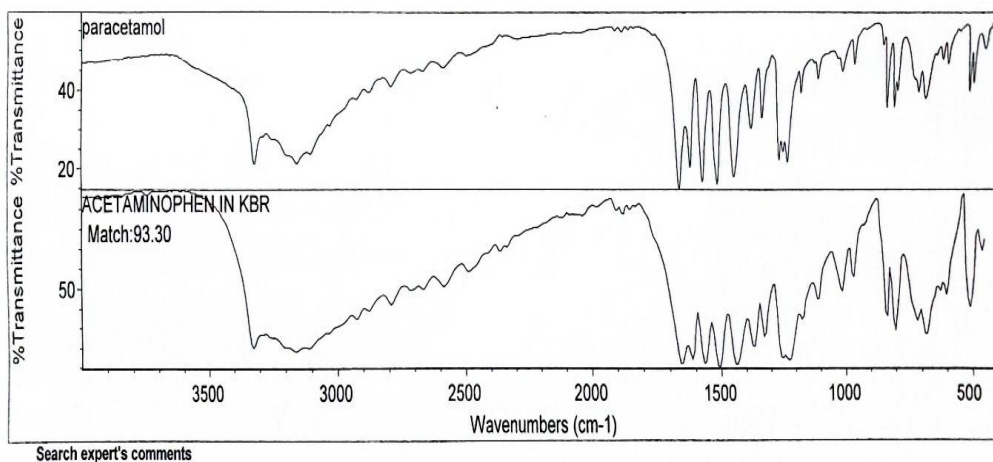
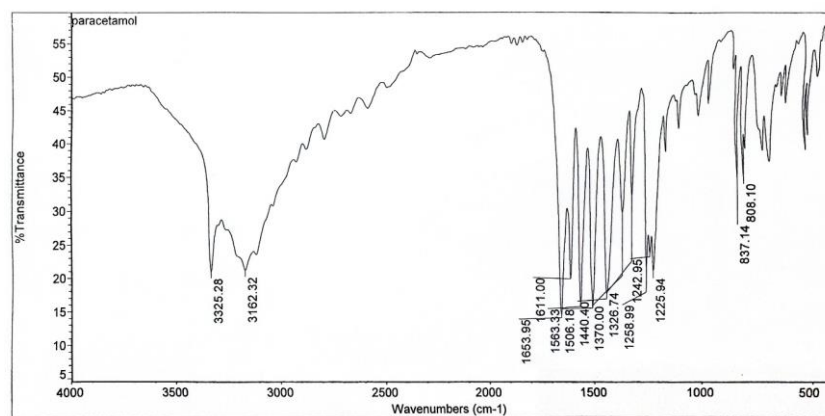


Fig. 5: FTIR Spectrum of Paracetamol STD.



**Fig. 6: FTIR Spectrum of Paracetamol.**

## CONCLUSION

The compatibility studies of physical mixtures of Azithromycin and Paracetamol with different used excipients such as PEG4000 base, and Witepsol were investigated by FTIR it was detected that there was no variation or minor deviation in the characteristic peaks in FTIR spectroscopy. The Azithromycin Dihydrate and Paracetamol formulations prepared were evaluated for preformulation parameters which were found to be within limits. It was concluded that the drug Azithromycin and Paracetamol was found to be compatible with various excipients which were selected for the formulation development of the Azithromycin and Paracetamol drugs in formulated suppositories Novel Drug Delivery Systems. Formulation scientist from his experience and knowledge have to significantly in the preformulation study stage and is an important factor in the NDDS (Novel Advanced Drug Delivery Systems) product development process.

## ACKNOWLEDGEMENT

The authors are thankful to Shaphaco Pharmaceutical Industry Company-Yemen, for support and facilities.

## REFERENCES

- World Health Organization (WHO). "Pneumonia". 2022.
- Malkawi, W. A., AlRafayah, E., AlHazabreh, M., AbuLaila, S., & Al-Ghananeem, A. M. Formulation Challenges and Strategies to Develop Pediatric Dosage Forms. *Children (Basel, Switzerland)*, 2022; 9(4): 488. <https://doi.org/10.3390/children9040488>.
- Bulić, M., & Tuleu, C. Rectal drug delivery to paediatric population. *Hrvatski časopis zdravstvenih znanosti*. 2021.
- Linakis, M.W., Roberts, J.K., Lala, A.C., Spigarelli, M.G., Medlicott, N.J., Reith, D.M., ... & Sherwin, C.M. Challenges associated with route of administration in neonatal drug delivery. *Clinical Pharmacokinetics*, 2016; 55: 185-196.
- Hua, S. Physiological and Pharmaceutical Considerations for Rectal Drug Formulation and Delivery. *Frontiers in Pharmacology*, 2019; 10: 1196. <https://doi.org/10.3389/fphar.2019.01196>.
- Langtry, H.D., & Balfour, J.A. Azithromycin: A review of its use in paediatric infectious diseases. *Drugs*, 1998; 56: 273-297.
- CARE Hospitals. Azithromycin: Uses, Dosage, Precautions and More. 2023. <https://www.carehospitals.com/medicine-detail/azithromycin>
- Drugs.com. Azithromycin and Paracetamol Interactions. 2023. <https://www.drugs.com/drug-interactions/azithromycin-with-paracetamol-300-0-11-2744.html>
- Abdulaziz, S. M., Abdulhamid, A. J., Abobakr, F. A., & Rajab, N. F. Antibacterial Activity of Paracetamol, Trimethoprim/sulfamethoxazole, Azithromycin, and Ciprofloxacin. *Journal of Advanced Zoology*. 2023.
- Basa, M., & Sovtić, A. Treatment of the most common respiratory infections in children. *Archives of Pharmacy*, 2022; 72: 118-133.
- Allen, L. V., & Ansel, H. C. *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems* (10th ed.). Lippincott Williams & Wilkins .2013.
- Bergogne-Bérézin, E., & Bryskier, A. The suppository form of antibiotic administration: pharmacokinetics and clinical application. *Journal of Antimicrobial Chemotherapy*, 1999; 43(2): 177-185.
- Kauss, T., Gaubert, A., Boyer, C., Ba, B. B., Manse, M., Massip, S., & Millet, P. Pharmaceutical development and optimization of azithromycin suppository for paediatric use. *International Journal of Pharmaceutics*, 2013; 441(1-2): 218-226.
- Kauss, T., Gaudin, K., Gaubert, A., Ba, B., Tagliaferri, S., Fawaz, F., ... & Millet, P. Screening paediatric rectal forms of azithromycin as an alternative to oral or injectable treatment. *International Journal of Pharmaceutics*, 2012; 436(1-2): 624-630.
- United States Pharmacopeia and National Formulary (USP 46-NF 41). *United States Pharmacopeial Convention*. 2023.
- Rowe, R. C., Sheskey, P. J., & Quinn, M. E. (Eds.). *Handbook of Pharmaceutical Excipients* (7th ed.). Pharmaceutical Press and American Pharmacists Association .2012.

17. IOI Oleo GmbH. (n.d.). WITEPSOL®: Hard fats for suppositories and ovules [Brochure]. Retrieved June 3, 2025, from [https://www.ioioleo.de/wp-content/uploads/2020/03/IOI\\_Oleo\\_Pharma\\_WITEPSOL.pdf](https://www.ioioleo.de/wp-content/uploads/2020/03/IOI_Oleo_Pharma_WITEPSOL.pdf)
18. Garg, R., Gupta, G. D., & Goyal, A. Formulation and evaluation of fast dissolving tablets of an antihypertensive drug. *International Journal of Pharmaceutical Investigation*, 2012; 2(2): 88–93. <https://doi.org/10.4103/2230-973X.100048>
19. Kaewnopparat, S., Kaewnopparat, N., & Rojanapibulpun, J. Influence of disintegrants on physical properties and drug release from piroxicam suppositories using a Witepsol H15 base. *Pharmaceutical Development and Technology*, 2004; 9(2): 185–191. <https://doi.org/10.1081/PDT-120037483>
20. Gibson, M. (Ed.). *Pharmaceutical preformulation and formulation: A practical guide from candidate drug selection to commercial dosage form* (2nd ed.). Informa Healthcare. 2009.
21. <https://go.drugbank.com/drugs/DB00207>
22. <https://pubchem.ncbi.nlm.nih.gov/compound/Azithromycin-Dihydrate>
23. <https://go.drugbank.com/drugs/DB00316>
24. <https://pubchem.ncbi.nlm.nih.gov/compound/Acetaminophen>
25. El-Shaibany A, Noman MA, Alburyhi MM, Saif AA, et al. Pharmacological Insights and Pharmaceutical Formulations of *Pandanus odoratissimus* Peduncle and *Curcuma longa*: A Narrative Review of Therapeutic Applications from 2010 to 2025. *European Journal of Biomedical and Pharmaceutical Sciences*, 2026; 13(4): 375-381.
26. Al-Ghani AM, Alkhwilani MA, Alburyhi MM, Alwosabi A. Formulation and Evaluation of Yemeni *Zizyphus Spina-Christi* Leaves Extracts as Anti-Bacterial and Anti-Dandruff Serum. *European Journal of Pharmaceutical and Medical Research.*, 2024; 11(10): 40-46.
27. Mohamed YAS, Hamidaddin MA, Yahya TA, Alkhwilani MA, Alburyhi MM. Phytochemical and Physicochemical Analysis of Yemeni *Kalanchoe Marmorata* Baker. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2025; 14(9): 1024-1033.
28. Noman MA, Alburyhi MM, Saif AA. Knowledge, Attitude and Practice Regarding the Proper Use, Risks and Resistance of Antibiotics Among Undergraduate Level Medical and Health Sciences Students in Sana'a, Yemen. *European Journal of Pharmaceutical and Medical Research.*, 2025; 12(12): 414-425.
29. El-Shaibany A, Alburyhi MM, Aoun MA, Ghallab HA. Pharmacological Evaluation of Marine Macroalgae from Yemeni Coastal Waters: Expanded Investigation into Their Antimicrobial and Antioxidant Activities. *World Journal of Pharmaceutical Research.*, 2025; 14(13): 1763-1770.
30. Al-Ghani AM, Alkhwilani MA, Alburyhi MM. Formulation Evaluation of Effect of Yemeni *Allium Sativum* (Garlic) in Treatment of Oral Candidiasis. *European Journal of Pharmaceutical and Medical Research.*, 2024; 11(8): 14-19.
31. Noman MA, Saif AA, Alburyhi MM. The Impact of Vitamin D Deficiency and Nutritional Habits on Height and Health Among Yemeni Adult Female Students in Sana'a, Yemen. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2026; 15(3): 855-875.
32. El-Shaibany A, Noman MA, Alburyhi MM, Saif AA, et al. *Punica granatum* Flower and *Hibiscus sabdariffa* Calyx: A Narrative Review of Phytochemistry, Antioxidant Mechanisms, and Therapeutic Potential. *World Journal of Pharmaceutical Research.*, 2026; 15(7): 1949-1966.
33. Alburyhi MM, El-Shaibany A, Al-Wajih AM, Alqadhi AA, Almlhani AN. Advancements in Nano-Formulation Systems for Enhancing the Delivery of Herbal Ingredients. *European Journal of Pharmaceutical and Medical Research.*, 2025; 12(1): 212-231.
34. Alburyhi MM, Moharram BA. Formulation and Evaluation of Aloe *Nieburhiana* Extract as Naturaceutical Effervescent Granules Novel Drug Delivery Systems for Antidiabetic Activity. *World Journal of Pharmaceutical Research.*, 2025; 14(18): 1147-1175.
35. Al-Ghorafi MA, Alburyhi MM, Muthanna MS. Chemical Incompatibilities of IV Admixture Combinations in ICU, Orthopedic and Emergency Units of Various Hospitals and Medical Centers in Sana'a, Yemen. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(10): 416-425.
36. Al-Ghorafi MA, Alburyhi MM. Formulation and Evaluation of Novel Antiaging Cream Containing Dragon's Blood Extract. *European Journal of Pharmaceutical and Medical Research.*, 2024; 11(1): 239-244.
37. Saif AA, Alburyhi MM, Noman MA, Almakhtari AM. Formulation and Evaluation of Trimetazidine Hydrochloride and Clopidogrel Bisulphate Multi-unit Solid Dosage Forms. *Journal of Chemical Pharm Research.*, 2014; 6(2): 421-426.
38. Othman AM, Alburyhi MM, Al-Hadad GH. Formulation and Stability Studies Evaluation of the Selected Captopril Mouth Dissolving Tablets MDTs. *World Journal of Pharmaceutical and Medical Research.*, 2025; 11(11): 275-284.
39. Raweh SM, Noman MA, Alburyhi MM, Saif AA. Formulation and Evaluation of Anti-acne Gel of *Azadirachta Indica* Extract Herbal Product. *European Journal of Pharmaceutical and Medical Research*, 2024; 11(2): 427-433.
40. El-Shaibany A, Noman MA, Alburyhi MM, Saif AA, et al. Global Burden, Pathophysiology, and Emerging Herbal Management Strategies for Diabetic Foot Ulcers: A Narrative Review. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2026; 15(4): 1130-1138.

41. Noman MA, Alburyhi MM, Saif AA, Yahya TAA. Formulation and Evaluation of Polyherbal Extract for Skin Hyperpigmentation as Gel Advanced Delivery Systems. *World Journal of Pharmaceutical Research.*, 2024; 13(22): 1260-1280.
42. Saif AA, Noman MA, Alburyhi MM. Formulation and Evaluation of Salicylic Acid and Kojic Acid as Gel Novel Drug Delivery Systems for Treatment of Acne and Whitening Skin Effect. *World Journal of Pharmaceutical and Medical Research.*, 2025; 11(9): 538-548.
43. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Vera Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(4): 1408-1423.
44. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Antitumor Activity of Artemisia Arborescence Extract Capsules as Dietary Supplement Herbal Product Against Breast Cancer. *World Journal of Pharmaceutical Research.*, 2024; 13(3): 95-114.
45. Saif AA, Noman MA, Alburyhi MM, Yahya TAA. Evaluation and Drug Stability Studies Some Levocetirizine Tablets Brands Available in Sana'a Market Yemen. *World Journal of Pharmaceutical Research.*, 2024; 13(24): 1009-1022.
46. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Vera Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. *World Journal of Pharmaceutical Research.*, 2024; 13(8): 1052-1072.
47. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Dictyota Dichotoma Extract Medicinal Seaweed Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. *European Journal of Biomedical and Pharmaceutical Sciences.*, 2024; 11(4): 63-70.
48. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Celery Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Gout. *World Journal of Pharmaceutical Research.*, 2024; 13(11): 2383-2404.
49. Othman AM, Alburyhi MM, Al-Hadad GH. Formulation and Evaluation of Captopril Mouth Dissolving Tablets. *European Journal of Pharmaceutical and Medical Research*, 2024; 11(1): 18-28.
50. El-Shaibany A, Noman MA, Alburyhi MM, Saif AA, et al. The Evolution and Therapeutic Potential of Polyherbal Gels and Key Botanical Extracts in Diabetic Foot Ulcer Management: A Comprehensive Narrative Review. *European Journal of Biomedical and Pharmaceutical Sciences*, 2026; 13(4): 368-374.
51. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Effervescent Granules of Artemisia Arborescence Herbal Product for Foodborne Illness. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2023; 12(12): 1429-1444.
52. Alburyhi MM, Noman MA, Saif AA, Alemad AF. Dispersible and Orodispersible Tablets Delivery Systems for Antibacterials Development. *World Journal of Pharmaceutical Research.*, 2025; 14(1): 1229-1257.
53. Noman MA, Alburyhi MM, Saif AA, Yahya TAA. Evaluation and Drug Stability Studies Some Atorvastatin Tablets Brands Available in Sana'a Market Yemen. *World Journal of Pharmaceutical and Medical Research.*, 2024; 10(12): 231-236.
54. Noman MA, Alburyhi MM, Saif AA. Knowledge and Perception about Pharmacovigilance Among 4Th and 5Th Levels Pharmacy Students in Some Public and Private Universities, Sana'a Yemen. *World Journal of Pharmaceutical and Medical Research.*, 2023; 9(11): 14-19.
55. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Anti-peptic Ulcer Capsules of Curcuma Longa Herbal Product. *World Journal of Pharmaceutical Research.*, 2023; 12(22): 76-96.
56. Noman MA, Alburyhi MM, El-Shaibany A, Alwesabi NA. Preformulation and Characterization Studies of Pandanus Odoratissimus L Extract Active Ingredient in Treatment of Nocturnal Enuresis. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(2): 1603-1620.
57. Othman AM, Alburyhi MM, Al-Hadad GH. Captopril-Excipient Preformulation Studies for Mouth Dissolving Tablets Development. *World Journal of Pharmaceutical Research*, 2025; 14(10): 1398-1420.
58. Alburyhi MM, Saif AA, Noman MA, Al-Ghorafi MA. Comparative Study of Certain Commercially Available Brands of Paracetamol Tablets in Sana'a City, Yemen. *European Journal of Pharmaceutical and Medical Research.*, 2018; 5(12): 36-42.
59. Noman MA, Alburyhi MM, El-Shaibany A, Alwesabi NA. Formulation and Evaluation of Pandanus Odoratissimus L Extract for Treatment of Nocturnal Enuresis as Orodispersible Tablets Delivery System. *World Journal of Pharmaceutical Research.*, 2024; 13(5): 56 -71.
60. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Tribulus Terrestris Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. *World Journal of Pharmaceutical Research.*, 2024; 13(7): 1264-1282.
61. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Pandanus Odoratissimus Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Hepatoprotective. *European Journal of Pharmaceutical and Medical Research.*, 2024; 11(4): 06-13.
62. El-Shaibany A, Noman MA, Alburyhi MM, Saif AA, et al. A Hepatoprotective and Anti-inflammatory Polyherbal Approach: The Synergistic

- Potential of *Acalypha fruticosa* and *Tribulus terrestris* Extract. *European Journal of Pharmaceutical and Medical Research.*, 2026; 13(4): 520-524.
63. Saif AA, Alburyhi MM, Noman MA. Evaluation of Vitamin and Mineral Tablets and Capsules in Yemen Market. *Journal of Chemical Pharma Research.*, 2013; 5(9): 15-26.
64. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of *Plicosepalus Acacia* Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Hepatoprotective. *World Journal of Pharmaceutical Research.*, 2025; 14(8): 1309-1334.
65. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Oral Pharmaceutical Solution of *Pandanus Odoratissimus* L Extract Herbal Product in Treatment of Nocturnal Enuresis. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(1): 1840-1851.
66. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Antibacterial Orodispersible Tablets of *Artemisia Arborescence* Extract Herbal Product. *European Journal of Pharmaceutical and Medical Research.*, 2024; 11(2): 409-417.
67. Al Ghoury AA, Al-Ghorafi MA, Alburyhi MM, Noman MA. Antimicrobial Susceptibility Patterns of *Staphylococcus Aureus* to Different Antimicrobial Agents Isolated as Clinical Samples at Certain General Hospitals in Sana'a City, Yemen. *World Journal of Pharmaceutical Research.*, 2024; 13(16): 35-47.
68. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of *Acalypha Fruticosa* Extract Tablets Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. *World Journal of Pharmaceutical Research.*, 2024; 13(8): 1073-1091.
69. Noman MA, Alburyhi MM, Saif AA, Yahya TAA. Assessment of Knowledge, Attitude, and Practice of Pharmacovigilance Among Pharmacists and Health care Professionals in Four Government Hospitals at Sana'a City, Yemen. *European Journal of Biomedical and Pharmaceutical Sciences.*, 2025; 12(5): 250-267.
70. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Ginger Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. *World Journal of Pharmaceutical and Medical Research.*, 2025; 11(6): 400-415.
71. Noman MA, Alburyhi MM, Yahya TAA, Saif AA. Evaluation and Drug Stability Studies of Different Brands of Clopidogrel Tablets Available in Sana'a City Market, Yemen. *European Journal of Biomedical and Pharmaceutical Sciences.*, 2025; 12(7): 181-191.
72. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of *Plicosepalus Acacia* Extract Capsules as Naturaceutical Novel Drug Delivery Systems for Controlling Diabetes. *World Journal of Pharmaceutical and Life Sciences.*, 2025; 11(6): 323-337.
73. Alburyhi MM, El-Shaibany A. Recent Innovations of Novel Drug Delivery Systems for Formulation, Development and Evaluation of *Pandanus Odoratissimus* Extract Capsules as Naturaceutical for Breast Cancer. *World Journal of Pharmaceutical Research.*, 2024; 13(8): 1092-1112.
74. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of *Tribulus Terrestris* Extract Capsules as Naturaceutical Novel Drug Delivery Systems for Kidney Stones. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(5): 1425-1443.
75. El-Shaibany A, Noman MA, Alburyhi MM, Saif AA, et al. Pharmacological and Formulation Advances in the Management of Hepatic and Inflammatory Disorders: A Review of *Acalypha fruticosa* and *Tribulus terrestris*. *World Journal of Pharmaceutical and Life Sciences.*, 2026; 12(4): 260-264.
76. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of *Capsicum* Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Tonic and Natural Stimulant. *European Journal of Pharmaceutical and Medical Research.*, 2025; 11(6): 323-337.
77. Alburyhi MM, Raweh SM, AlGhoury ABA, Alkhwilani MA, Noman MA, Saif AA. Recent Innovations of Novel Drug Delivery Systems for Formulation, Development and Evaluation of *Grewia Tenax* Extract Naturaceutical Ointment for Antimicrobial Activity. *World Journal of Pharmaceutical and Medical Research.*, 2025; 11(7): 413-426.
78. Alburyhi MM, Raweh SM, Al-Ghorafi MA, Saif AA, Noman MA. Formulation and Evaluation of *Argemone Ochroleuca* Extract Cream Naturaceutical Delivery Systems as Antimicrobial and Wound Healing Activity. *European Journal of Pharmaceutical and Medical Research.*, 2025; 12(7): 445-459.
79. Mohamed YAS, Alkhwilani MA, Wadi ZAS, Yahya TAA, Faisal A, Alburyhi MM. Modern Analytical Techniques for Authentication of Yemeni Ambergris. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2025; 14(8): 686-697.
80. Alburyhi MM, Mohamed YAS. Formulation, Development and Evaluation of Cosmeceutical Natural Pigmented Lipstick from *Opuntia Dillenii* Fruit Extract. *European Journal of Biomedical Pharmaceutical and Medical Sciences.*, 2025; 12(9): 466-479.
81. El-Shaibany A, Noman MA, Alburyhi MM, Saif AA, et al. Synergistic Potential of *Pandanus odoratissimus* and *Curcuma longa* in the Management of Nocturnal Enuresis: A Comprehensive Narrative Review of Botanical, Pharmacological, and Formulation Strategies. *World*

- Journal of Pharmaceutical Research., 2026; 15(7): 1934-1948.
82. Al-Ghorafi MA, Alburyhi MM, Muthanna MS. Effect of Rosemary and Myrtus Extracts Combination on Androgenetic Alopecia: A Comparative Study with Minoxidil. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(10): 35-39.
83. Alburyhi MM, El-Shaibany A, Al-Wajih AM, Almlhani AN, Alqadhi AA. Innovative Approaches in Herbal Drug Delivery Systems Enhancing Efficacy and Reducing Side Effects. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2025; 14(1): 919-929.
84. Alburyhi MM, Moharram BA. Formulation and Evaluation of *Jatropha Variiegata* Extract as Antibacterial Naturaceutical Cream Novel Drug Delivery Systems for Wound Healing Activity. *World Journal of Pharmaceutical and Life Sciences.*, 2025; 11(10): 177-190.
85. Noman MA, Alburyhi MM, Saif AA. Formulation and Evaluation of Skin Whitening Naturaceutical Composition Gel as Advanced Drug Delivery Systems. *World Journal of Pharmaceutical and Medical Research*, 2025; 11(10): 400-414.
86. El-Shaibany A, Noman MA, Alburyhi MM, Saif AA, et al. *Punica granatum* Flower and *Hibiscus sabdariffa* Calyx: A Narrative Review of Phytochemistry, Antioxidant Mechanisms, and Synergistic Potential in Oxidative Stress Management. *World Journal of Pharmaceutical and Medical Research.*, 2026; 12(4): 418-427.
87. Al-Samawi HM, El-Shaibany A, Alburyhi MM. Review Article: The Therapeutic Potential of *Micromeria Biflora*: A Comprehensive Review. *World Journal of Pharmaceutical Research.*, 2024; 13(6): 7-11.
88. Alburyhi MM, Moharram BA. Formulation and Evaluation of Aloe Inermis Extract for Wound Healing Activity as Antibacterial Naturaceutical Cream Novel Drug Delivery Systems. *European Journal of Pharmaceutical and Medical Research.*, 2025; 12(10): 297-308.
89. Al-Wajih AM, El-Shaibany A, Alburyhi MM, Abdelkhalek AS, Elaasser MM, Raslan AE. Comparative Study of Phytochemical Composition, Oral Toxicity, Antioxidant, and Anticancer Activities of Both *Aloe Vera* and *Aloe Vacillans* (Asphodelaceae Family) Flowers Extract: In Vitro, In Vivo, and in Silico Studies. *Trends in Phytochemical Research.*, 2025; 9(1): 1-22.
90. Al-Samawi HM, El-Shaibany A, Alburyhi MM. Review Article: The Pharmacological Potential of The Genus *Micromeria*. *World Journal of Pharmaceutical Research.*, 2024; 13(6): 1-6.
91. Noman MA, Alburyhi MM, Saif AA. Effect of Chewing Khat on Nutritional Status Among Female Students at Undergraduate Level in Sana'a, Yemen. *World Journal of Pharmaceutical Research.*, 2023; 12(20): 75-88.
92. Al-Samawi HM, El-Shaibany A, Alburyhi MM. Review Article: Phytochemistry and Pharmacological Activities of *Micromeria* Species. *World Journal of Pharmaceutical Research.*, 2024; 13(15): 1335-1347.
93. Sravani M. Formulation and Evaluation of Mouth Dissolving Tablets of Nebivolol HCl for Treatment of Hypertension. *Int J Pharma Chem Res.*, 2017; 3: 200-212.
94. Gandhi L, Akhtar MS. Comparative Study on Effect of Natural and Synthetic Superdisintegrants in the Formulation of Orodispersible Tablets. *J Drug Deliv. Ther.*, 2019; 9(2): 507-513.
95. Santosh Kumar R, Kumari A. Fast Dissolving Tablets: Waterless Patient Compliance Dosage Forms. *J Drug Deliv Ther.*, 2019; 9(1): 303-317.
96. Raymond CR, Paul JS, Marian EQ. Handbook of Pharmaceutical Excipients, 6th Edition. Pharmaceutical Press and American Pharmacists Association., 2009; S48-S760.
97. Vishali T, Damodharan N. Orodispersible Tablets: A Review. *Res. J. Pharm. Tech.*, 2020; 13(5): 2522-2529.
98. Nagar P, Singh K, Chauhan I, Verma M, Yasir M, Khan A, Sharma R, Gupta N. Orally disintegrating Tablets: Formulation, Preparation Techniques and Evaluation. *J. Appl. Pharm. Sci.*, 2011; 35-45.
99. Sivagurunathan D. Formulation and *In-Vitro* Evaluation of Rivaroxaban Immediate Release Tablets: An Approach to Improving Oral Bioavailability Using Solid Dispersion Technique. The Tamil Nadu Dr. M.G.R. Medical University., 2020; 600032.
100. Sandhyarani G, Sarangapani M. Formulation and Evaluation of Orodispersible Tablets of Domperidone. *IOSR J Pharm.*, 2016; 6(9): 39-47.
101. Upadhyay P, et al. A Review on Formulation and Evaluation Approaches for Fast Release Tablet. *Mathews J Pharma Sci.*, 2023; 7(1): 15.
102. Ramu S, Kumar YA, Rao DS, Ramakrishna G. Formulation and Evaluation of Valsartan Oral Dispersible Tablets by Direct Compression Method. *Am J. Adv. Drug Deliv.*, 2014; 1: 2321-547X.
103. Pankaj M. A Discriminatory Drug Dissolution Method for Estimation of Rivaroxaban from Rivaroxaban Tablets. *Scholars Res Library Der. Pharmacia. Lett.*, 2019; 11(2): 97-103.
104. Gupta H, Bhandari D, Sharma A. Recent Trends in Oral Drug Delivery: A Review. *Recent Pat Drug Deliv Formul.*, 2009; 3: 162-173.
105. Kakar S, Singh R, Kumar S. Orodispersible Tablets: an Overview. *MOJ Proteomics Bioinform.*, 2018; 7(3): 180-182.
106. Hirani JJ, Rathod DA, Vadalia KR. Orally Disintegrating Tablets: A Review. *Trop. J. Pharm. Res.*, 2009; 8(2): 161-172.
107. Gupta DK, Maurya A, Varshney MM. Orodispersible Tablet: An Overview of Formulation and Technology. *World J Pharm. Pharm. Sci.*, 2020; 9(2): 1408.

108. Pandya P, Dahiya M. Oral disintegrating Tablets: A Review. *Int J Pharma Res.*, 2016; 5(1): 51.
109. Bhowmik D, Chiranjib B, Krishnath P, Chaandira RM. Fast Dissolving Tablet: an Overview. *J. Chem. Pharm. Res.*, 2009; 1(1): 165.
110. Arora P, Sethi VA. Orodispersible Tablet: a Comprehensive Review. *Int J Res Drug Dev Pharm Life Sci.*, 2013;2(2):271-272.
111. Jassem NA. Orodispersible Tablets: a Review on Recent Trends in Drug Delivery. *IJDDT.*, 2022; 12: 433.
112. Nehal SM, Garima G, Pramod KS. Fast Dissolving Tablets: Preparation, Characterization and Evaluation: an Overview. *Int. J. Pharm. Sci. Rev. Res.*, 2015; 31(2): 243-250.
113. Deshmukh H, Chandrashekhara S, Nagesh C, Murade A, Usgaunkar S. Superdisintegrants: a Recent Investigation and Current Approach. *Asian J. Pharm. Tech.*, 2012; 2: 19-25.
114. Abha, Kaur LP. Superdisintegrations: an Arising Exemplar in Orodispersible Tablets. *Int J Drug Res Technol.*, 2015; 5(1): 1-12.
115. Patil NC, Raja K. Formulation and Evaluation of Orodispersible Tablets of Metoclopramide Hydrochloride. *Tamilnadu Dr.M.G.R. Medical University.*, 2012; 638-652.
116. *Drug Information Handbook: a Comprehensive Resource for All Clinicians and Healthcare Professionals.* 21st ed. American Pharmacist Association and Lexi-Comp., 2012; S1620.
117. BNF. *BMJ Group and Royal Pharmaceutical Society.* September 2022-March 2023; 140-S141.
118. Preston CL. *Stockley's Drug Interaction Pocket Companion.* 2nd ed. Pharmaceutical Press., 2015; S119-S576.
119. Borse LB, Bendale AR, Borse SL, Naphade VD, Jadhav AG. Formulation and Evaluation of Mouth Dissolving Tablet Rivaroxaban and its Validation. *Biosci Biotechnol Res Asia.*, 2022; 19(4): 943-954.
120. Stuart BH. *Infrared Spectroscopy: Fundamentals and Applications.* 1st ed. Wiley., 2004; S168.
121. Bharate SS, Bharate SB, Bajaj AN. Interactions and Incompatibilities of Pharmaceutical Excipients with Active Pharmaceutical Ingredients: A Comprehensive Review. *J Excip Food Chem.*, 2010; 1: 3-26.
122. Moyano MA, Broussalis AM, Segall A. Thermal Analysis of Lipoic Acid and Evaluation of the Compatibility with Excipients. *J Therm Anal Cal.*, 2010; 99: 631-637.
123. Ceresole R, Han Y, Rosasco MA, Orelli LR, Segall AI. Drug-Excipient Compatibility Studies in Binary Mixtures of Avobenzone. *J Cosmet Sci.* 2013; 64: 317-328.
124. Chadha R, Bhandari S. Drug-Excipient Compatibility Screening—Role of Thermoanalytical and Spectroscopic Techniques. *J Pharm Biomed Anal.*, 2014; 87: 82-97.
125. McDaid FM, Barker SA, Fitzpatrick S, Petts C, Craig DQM. Further Investigations into The Use of High Sensitivity Differential Scanning Calorimetry as A Means of Predicting Drug-Excipient Interactions. *Int J Pharm.*, 2003; 252: 235-240.
126. O'Neill MA, Gaisford S. Application and Use of Isothermal Calorimetry in Pharmaceutical Development. *Int J Pharm.*, 2011; 417: 83-93.
127. Ferraz Pinto M, Afonso de Moura E, Santos de Souza F, Oliveira Macêdo R. Thermal Compatibility Studies of Nitroimidazoles and Excipients. *J Therm Anal Cal.*, 2010; 102: 323-329.
128. Oliveira Santos AF, Basilio Jr ID, Souza FS, Medeiros AFD, Ferraz Pinto M, de Santana DP. Application of Thermal Analysis of Binary Mixtures with Metformin. *J Therm. Anal Cal.*, 2008; 93: 361-364.
129. Chou YP, Huang JY, Tseng JM, Cheng Y, Shu CM. Reaction Hazard Analysis for The Thermal Decomposition of Cumene Hydroperoxide in The Presence of Sodium Hydroxide. *J Therm Anal Cal.*, 2008; 93: 275-280.
130. Sashima ES, Janowska G, Zaborski M, Vnuchkin AV. Compatibility of Fibroin/Chitosan and Fibroin/Cellulose Blends by Thermal Analysis. *J Therm Anal Cal.*, 2007; 89:887-891.
131. Medeiros AFD, Santos AFO, de Souza FS, Júnior IDB, Valdilânio J, Procópio JVV, de Santana DP, Macêdo RO. Thermal Studies of Preformulates of Metronidazole Obtained by Spray Drying Technique. *J Therm. Anal. Cal.*, 2007; 89: 775-781.
132. Silva MAS, Kelmann RG, Foppa T, Cruz AP, Bertol CD Sartori T, Granada A, Carmignan F, Murakami FS. Thermoanalytical Study of Fluoxetine Hydrochloride. *J. Therm. Anal. Cal.*, 2007; 87: 463-467.
133. Lira AM, Araújo AAS, Basílio IDJ, Santos BLL, Santana DP, Macêdo RO. Compatibility Studies of Lapachol with Pharmaceutical Excipients for The Development of Topical Formulations. *Thermochim. Acta.*, 2007; 457: 1- 6.
134. Mura P, Furlanetto S, Cirri M, Maestrelli F, Marras AM, Pinzauti S. Optimization of Glibenclamide Tablet Composition Through the Combined Use of Differential Scanning Calorimetry and D-Optimal Mixture Experimental Design. *J. Pharm. Biomed. Anal.*, 2005; 37: 65-71.
135. Araújo AAS, Storpirtis S, Mercuri LP, Carvalho FMS, dos Santos Filho M, Matos JR. Thermal Analysis of The Antirretroviral zidovudine (AZT) and Evaluation of The Compatibility with Excipients Used in Solid Dosage Forms. *Int. J. Pharm.*, 2003; 260: 303-314.
136. Matos APS, Costa JS, Boniatti J, Seiceira RC, Pitaluga Jr A, Oliveira DL, Visçosa AL, Holandino C. Compatibility Study Between Diazepam and Tablet Excipients. *J. Therm. Anal. Cal.*, 2017; 127: 1675-1682.
137. Liltorp K, Larsen TG, Willumsen B, Holm R. Solid State Compatibility Studies with Tablet Excipients Using Non Thermal Methods. *J Pharm Biomed Anal.*, 2011; 55: 424-428.

138. Verma RK, Garg S. Selection of Excipients for Extended-Release Formulations of Glipizide Through Drug-Excipient Compatibility Testing. *J Pharm Biomed Anal.*, 2005; 38: 633-644.
139. Verma RK, Garg S. Compatibility Studies between Isosorbide Mononitrate and Selected Excipients Used in The Development of Extended-Release Formulations. *J Pharm. Biomed. Anal.*, 2004; 35: 449-458.
140. Silva LAD, Teixeira FV, Serpa RC, Esteves NL, dos Santos RR, Lima EM, da Cunha-Filho MSS, de Souza Araújo AA, Taveira SF, Marreto RN. Evaluation of Carvedilol Compatibility with Lipid Excipients for The Development of Lipid-Based Drug Delivery Systems. *J Therm. Anal. Cal.*, 2016; 123: 2337-2344.
141. Veiga A, Oliveira PR, Bernardi LS, Mendes C, Silva MAS, Sangoi MS, Janissek PR, Murakami FS. Solid-State Compatibility Studies of A Drug Without Melting Point. *J. Therm. Anal. Cal.*, 2018; 131: 3201-3209.
142. Rus. LM, Tomuta I, Iuga C, Maier C, Kacso I, Borodi G, Bratu I, Bojita M. Compatibility Studies of Indapamide/Pharmaceutical Excipients Used in Tablet Preformulation. *Farmacia.*, 2012; 60: 92-101.
143. Tomassetti M, Catalani A, Rossi V, Vecchio S. Thermal Analysis Study of The Interactions between Acetaminophen and Excipients in Solid Dosage Forms and in Some Binary Mixtures. *J Pharm Biomed Anal.*, 2005; 35: 949-955.
144. Ding T, Chen L, Zhai LH, Fu Y, Wang-Sun B. Compatibility Study of Rivaroxaban and Its Pharmaceutical Excipients. *J Therm. Anal. Cal.*, 2017; 130: 1569-1573.
145. Pires SA, Mussel WN, Yoshida MI. Solid-State Characterization and Pharmaceutical Compatibility between Citalopram and Excipients Using Thermal and Non-Thermal Techniques. *J. Therm. Anal. Cal.*, 2017; 127: 535- 542.
146. Joshi BV, Patil VB, Pokharkar VB. Compatibility Studies between Carbamazepine and Tablet Excipients Using Thermal and Non-Thermal Methods. *Drug Devel. Ind. Pharm.*, 2002; 28: 687-694.
147. Stulzer HK, Rodrigues PO, Cardoso TM, Matos JSR, Silva MAS. Compatibility Studies between Captopril and Pharmaceutical Excipients Used in Tablets Formulations. *J Therm. Anal Cal.*, 2008; 9: 323-328.
148. Bary AA, El-Gazayerly ON, Alburyhi MM. A Pharmaceutical Study on Lamotrigine. Ph.D. Thesis, Faculty of Pharmacy, Cairo University., 2009.
149. Saif AA, Alburyhi MM, Noman MA. Ketoprofen-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2025; 14(4): 92-123.
150. Alburyhi MM, Saif AA, Noman MA, Yassin SH. Formulation and Evaluation of Simvastatin Orodispersible Tablets. *World Journal of Pharmaceutical Research.*, 2023;12(16): 1033-1047.
151. Alburyhi MM, Saif AA, Noman MA, Al Ghoury AA. Formulation and Evaluation of Antimalarial Drugs Suppositories. *World Journal of Pharmaceutical Research.*, 2023; 12(20): 89-108.
152. Alburyhi MM, Yahya TAA, Saif AA, Noman MA, Alshoba N, Saeed SA. Acyclovir-Excipient Compatibility Studies for Gel Novel Drug Delivery Systems Development. *World Journal of Pharmaceutical Research.*, 2026; 15(6): 1247-1292.
153. Alburyhi MM, Saif AA, Noman MA, Saeed SA, Al-Ghorafi MA. Formulation and Evaluation of Diclofenac Orodispersible Tablets. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(9): 01-06.
154. Saif AA, Alburyhi MM, Noman MA. Formulation and Evaluation of Ketoprofen Fast Dissolving Tablets. *International Journal of Sciences.*, 2018; 7(09):27- 39.
155. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Chamomile Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Gout. *World Journal of Pharmaceutical and Life Sciences.*, 2025; 11(04): 215-228.
156. Alburyhi MM, Noman MA, Saif AA. Metronidazole-Excipient Compatibility Studies for Medicated Chewing Gum Delivery Systems Development. *European Journal of Pharmaceutical and Medical Research.*, 2025; 12(4): 567-589.
157. Alburyhi MM, Saif AA, Noman MA, Alkhawlani MA. Formulation and Evaluation of Bisoprolol Fast Dissolving Tablets. *World Journal of Pharmaceutical Research.*, 2023;12(16): 01-10.
158. Alburyhi MM, Noman MA, Saif AA, Salim YA, Abdullah JH. Formulation and Evaluation of Domperidone Orodispersible Tablets. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(3): 49-68.
159. Alburyhi MM, Saif AA, Noman MA, Hamidaddin MA. Formulation and Evaluation of Clopidogrel Orodispersible Tablets. *World Journal of Pharmaceutical Research.*, 2024; 13(6): 42-64.
160. Alburyhi MM, Saif AA, Noman MA, Al Khawlani MA. Bisoprolol-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmaceutical and Medical Research.*, 2024; 10(10): 304-324.
161. Saif AA, Abdullah JH, Alburyhi MM, Noman MA, Saeed SA. Sildenafil-Excipient Compatibility Studies for Pharmaceutical Oral Suspensions Advanced Drug Delivery Systems Development. *World Journal of Pharmaceutical Research.*, 2026; 15(6): 869-908.
162. Saif AA, Alburyhi MM, Noman MA, Abudunia A. Amoxicillin-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. *European Journal of Pharmaceutical and Medical Research.*, 2025; 12(6): 530-562.

163. Alburyhi MM, Mohamed YAS, Saif AA, Noman MA, Abdullah JH, Yahya TAA. Recent Innovations of Novel Drug Delivery Systems for Formulation, Development and Evaluation of Amlodipine and Furosemide Orodispersible Tablets. *World Journal of Pharmaceutical and Medical Research*, 2025; 11(5): 358-378.
164. Alburyhi MM, Mohamed YAS, Saif AA, Noman MA. Compatibility Studies with Pharmaceutical Excipients of Amlodipine for the Development of Novel Delivery Systems. *World Journal of Pharmacy and Pharmaceutical Sciences*, 2024; 13(11): 95-136.
165. Alburyhi MM, Saif AA, Noman MA. Compatibility Studies with Pharmaceutical Excipients of Clopidogrel for the Development of Novel Delivery Systems. *World Journal of Pharmaceutical Research*, 2025; 14(06): 1448-1486.
166. Alburyhi MM, Saif AA, Noman MA. Compatibility Studies of Pyrimethamine with Pharmaceutical Excipients for the Development of Suppositories Novel Drug Delivery Systems. *European Journal of Pharmaceutical and Medical Research*, 2025; 12(9): 394-412.
167. Alburyhi MM, Saif AA, Noman MA, Abudunia A, Yassin SH, Abdullah JH. Formulation, Development and Evaluation of Amoxicillin Fast Dissolving Tablets. *World Journal of Pharmaceutical and Life Sciences*, 2025; 11(7): 183-197.
168. Alburyhi MM, Salim YA, Saif AA, Noman MA. Furosemide-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmaceutical Research*, 2024; 13(22): 1178-1219.
169. Alburyhi MM, Saif AA, Noman MA. Lornoxicam-Excipient Compatibility Studies for Microsponge-Based Drug Delivery Systems Development. *World Journal of Pharmaceutical and Medical Research*, 2025; 11(4): 70-81.
170. Alburyhi MM, Noman MA, Saif AA. Formulation and Evaluation of Natural Herbal Anti-acne as Gel Delivery Systems. *World Journal of Pharmaceutical Research*, 2024; 13(21): 1447-1467.
171. Alburyhi MM, Yahya TAA, Saif AA, Noman MA. Formulation and Evaluation of Lornoxicam Microsponge-Based Gel as A Transdermal Drug Delivery Systems. *World Journal of Pharmaceutical and Life Sciences*, 2025; 11(5): 200-217.
172. Alburyhi MM, Hamidaddin MA, Noman MA, Saif AA. Recent Innovations of Novel Drug Delivery Systems for Formulation, Development and Evaluation of Metronidazole Medicated Chewing Gum Tablets. *European Journal of Biomedical and Pharmaceutical Sciences*, 2025; 12(6): 353-370.
173. Alburyhi MM, Noman MA, Saif AA, Al-Ghorafi MA, Al Khawlani MA, Yahya TAA. Formulation and Evaluation of Anti-acne Spironolactone Emulgel Novel Trend in Topical Drug Delivery System. *World Journal of Pharmaceutical Research*, 2023; 12(22): 96-119.
174. Alburyhi MM, Noman MA, Saif AA, Salim YA, Hamidaddin MA, Yahya TA, Al-Ghorafi MA, Abdullah JH. Lisinopril-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmaceutical Research*, 2024; 13(16): 59-111.
175. Alburyhi MM, Saif AA, Noman MA. Compatibility Studies of Sulfadoxine with Pharmaceutical Excipients for the Development of Suppositories Novel Drug Delivery Systems. *World Journal of Pharmaceutical and Life Sciences*, 2025; 11(9): 189-207.
176. Alburyhi MM, Saif AA, Noman MA, Saif RM. The Importance of Stability Testing in Pharmaceutical Development of Ceftriaxone Implant Biodegradable Tablets. *Matrix Science Pharma (MSP)*, 2025; 9(2): 58-63.
177. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Curcuma Longa Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. *European Journal of Biomedical and Pharmaceutical Sciences*, 2024; 11(6): 37-43.
178. Alburyhi MM, Saif AA, Noman MA, AlGhoury ABA. Compatibility Studies of Chloroquine Phosphate with Pharmaceutical Excipients for the Development of Suppositories Novel Drug Delivery Systems. *World Journal of Pharmaceutical Research*, 2025; 14(14): 1325-1360.
179. Alburyhi MM, Saif AA, Noman MA, Yassin SH. Compatibility Studies with Pharmaceutical Excipients of Simvastatin for the Development of Novel Drug Delivery Systems. *World Journal of Pharmaceutical Research*, 2024; 13(19): 1463-1512.
180. Hamidaddin MA, Alburyhi MM, Noman MA, Saif AA. Formulation and Evaluation of Rosuvastatin Fast Dissolving Tablets. *World Journal of Pharmacy and Pharmaceutical Sciences*, 2023; 12(9): 2293-2303.
181. Alburyhi MM, Hamidaddin MA, Noman MA, Saif AA, Yahya TA, Al-Ghorafi MA. Rivaroxaban-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *European Journal of Pharmaceutical and Medical Research*, 2024; 11(9): 370-404.
182. Alburyhi MM, Noman MA, Saif AA, Hamidaddin MA, Yahya TA, Al-Ghorafi MA. Rosuvastatin Calcium-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmaceutical Research*, 2024; 13(13): 1549-1582.
183. Bary AA, El-Gazayerly ON, Alburyhi MM. Formulation of Immediate Release Lamotrigine Tablets and Bioequivalence Study. *Journal of Chemical Pharm Research*, 2013; 5(10): 266-271.
184. Alburyhi MM, Saif AA, Noman MA. Stability Study of Six Brands of Amoxicillin Trihydrate and Clavulanic Acid Oral Suspension Present in Yemen Markets. *Journal of Chemical Pharm Research*, 2013; 5(5): 293-296.

185. Saif AA, Alburyhi MM, Noman MA, Yahya TA, Al-Ghorafi MA. Famotidine-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmaceutical Research.*, 2024; 13(18): 1346-1408.
186. Alburyhi MM, Saif AA, Noman MA, Yahya TA. Formulation, Development and Evaluation of Famotidine Orodispersible Tablets. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(10): 56-62.
187. Al-Ghorafi MA, Alburyhi MM, Saif AA, Noman MA, Yahya TA. Drotaverine-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmaceutical Research.*, 2024; 13(18): 1285-1340.
188. Alburyhi MM, Saif AA, Noman MA. Ticagrelor-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(10): 1081-1132.
189. Alburyhi MM, Noman MA, Saif AA, Al-Ghorafi MA, Yahya TA, Yassin SH, AlKhawlani MA. Diclofenac-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmaceutical Research.*, 2024; 13(14): 1297-1333.
190. Alburyhi MM, Saif AA, Noman MA, Salim YA, Hamidaddin MA. Formulation and Evaluation of Lisinopril Orally Disintegrating Tablets. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2023; 12(9): 357-369.
191. Alburyhi MM, Hamidaddin MA, Saif AA, Noman MA. Formulation and Evaluation of Rivaroxaban Orodispersible Tablets. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(2): 2066-2092.
192. Alburyhi MM, Saif AA, Noman MA, Saif RM. Recent Innovations of Delivery Systems for Antimicrobial Susceptibility Study of Ciprofloxacin Biodegradable Formulations for Post-Operative Infection Prophylaxis. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(9): 32-36.
193. Alburyhi MM, Noman MA, Aboghanem A. Effect of Different Excipients on Formulation of Immediate Release Artemether/Lumefantrine Tablets. *Journal of Chemical Pharm Research.*, 2013; 5(11): 617-625.
194. Alburyhi MM, Saif AA, Noman MA. Formulation and Evaluation of Ticagrelor Orodispersible Tablets. *World Journal of Pharmaceutical Research.*, 2024; 13(5): 26-55.
195. Alburyhi MM, Saif AA, Noman MA, Yahya TA, Al-Ghorafi MA. Formulation and Evaluation of Drotaverine Orally Disintegrating Tablets. *World Journal of Pharmaceutical Research.*, 2023; 12(18): 66-79.
196. Al-Ghorafi MA, Alburyhi MM, Saif AA, Noman MA. Meloxicam-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmaceutical and Medical Research.*, 2025; 11(1): 87-106.
197. Alburyhi MM, Saif AA, Saif RM. Preformulation Study of Ceftriaxone and Ciprofloxacin for Lipid Based Drug Delivery Systems. *EJUA-BA*, 2022; 3(4): 339-350.
198. Noman MA, Alburyhi MM, Alqubati MA. Preformulation and Characterization Studies of Clopidogrel Active Ingredient for Orodispersible Tablets Development. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(3): 996-1015.
199. Alburyhi MM, Noman MA, Alemad AF. Preformulation Studies of Cefixime for Dispersible Tablets Delivery System Development. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(12): 75-99.
200. Alburyhi MM, Noman MA, AA Saif. Formulation and Evaluation of Meloxicam Emulgel Delivery System for Topical Applications. *World Journal of Pharmaceutical Research.*, 2025; 14(4): 1324-1337.
201. Bary AA, El-Gazayerly ON, Alburyhi MM. A Pharmaceutical Study on Methocarbamol. MSc Thesis, Faculty of Pharmacy, Cairo University., 2006.
202. Alburyhi MM, Saif AA, Noman MA, Saeed SA. Compatibility Studies of Chlorhexidine with Pharmaceutical Excipients for the Development of Gel Novel Delivery Systems. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2026; 15(4): 1071-1109.
203. Alburyhi MM, Saif AA, Noman MA, Saif RM. Recent Innovations of Delivery Systems for Antimicrobial Susceptibility Study of Ceftriaxone Biodegradable Formulations for Post-Operative Infection Prophylaxis. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(8): 95-99.
204. Alburyhi MM, Saif AA, Noman MA. Domperidone-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Biomedical and Pharmaceutical Sciences.*, 2025; 12(3): 250-269.
205. Alburyhi MM, Saif AA, Noman MA. Spironolactone-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2025; 14(3): 871-910.
206. Jangde R, Singh D. Compatibility Studies of Quercetin with Pharmaceutical Excipients used in The Development of Novel Formulation. *Research J. Pharm. and Tech.*, 2014; 7: 1101-1105.
207. Tiwari SP, Vidyasagar G. Identification, Characterization, and Drug Excipient Compatibility of Diltiazem Hydrochloride by Physico-Chemical Techniques UK. *J. Pharm. Bio. Sci.*, 2014; 2: 49-53.
208. Gupta A, Kar HK. Solid State Compatibility Studies of Miconazole Using Thermal and Spectroscopic Methods. *Adv. Anal. Chem.*, 2015; 5: 51-55.

209. Khan MI, Madni A, Ahmad S, Khan A, Rehman M, Mahmood MA. ATRFTIR Based Pre and Post Formulation Compatibility Studies for The Design of Niosomal Drug Delivery System Containing Nonionic Amphiphiles and Chondroprotective Drug. *J Chem. Soc. Pak.*, 2015; 37: 527-534.
210. da Silva EP, Pereira MAV, de Barros Lima IP, Barros Lima NGP, Barboza EG, Aragã CFS, Gomes APB. Compatibility Study between Atorvastatin and Excipients Using DSC and FTIR. *J Therm Anal Cal.*, 2016; 123: 933- 939.
211. Amir IM, Amir ME, Osama AA, Suzan A, Alaa IM. Investigation of Drug–Polymer Compatibility Using Chemometric-Assisted UV Spectrophotometry. *Pharmaceutics.*, 2017; 9: 1-13.
212. Canbay HS, Doğantürk M. Application of Differential Scanning Calorimetry and Fourier Transform Infrared Spectroscopy to The Study of Metoprolol-Excipient and Lisinopril-Excipient Compatibility. *Eurasian., J Anal Chem.*, 2018; 13: 1-7.
213. Monajjemzadeh F, Hassanzadeh D, Valizadeh H, Siah-Shadbad MR, Mojarrad JS, Robertson TH, Roberts MS. Compatibility Studies of Acyclovir and Lactose in Physical Mixtures and Commercial Tablets. *Eur. J. Pharm. Biopharm.*, 2009; 73: 404-413.
214. Mura P, Manderioli A, Bramanti G, Furlanetto S, Pinzauti S. Utilization of Differential Scanning Calorimetry as A Screening Technique to Determine The Compatibility of ketoprofen with Excipients. *Int. J. Pharm.*, 1995; 119: 71-79.
215. Malan CEP, de Villiers MM, Lötter AP. Application of Differential Scanning Calorimetry and High-Performance Liquid Chromatography to Determine the Effects of Mixture Composition and Preparation During The Evaluation of Niclosamide-Excipient Compatibility. *J Pharm Biomed Anal.*, 1997; 15: 549-557.
216. Rojek B, Wesolowski M. Fourier Transform Infrared Spectroscopy Supported by Multivariate Statistics in Compatibility Study of Atenolol with Excipients. *Vib Spectrosc.*, 2016; 86: 190–197.
217. Prasanna Kumar et al. An Overview on Preformulation Studies. *Indo Am. J. Pharm. Sci.*, 2015; 2(10).
218. Allen L, Ansel H. *Pharmaceutical Dosage Forms and Drug Delivery Systems by Ansel (10th Edition)*. Lippincott Williams & Wilkins, Philadelphia., 2014.
219. Daniel JSP, Veronez IP, Lopez Rodriguez L, Trevisan MG, García JS. Risperidone – Solid-State Characterization and Pharmaceutical Compatibility Using Thermal and Non-Thermal Techniques. *Thermochim. Acta.*, 2013; 568: 148-155.
220. Lima NGPB, Lima IP, Barros DMC, Oliveira TS, Raffin FN, de Lima e Moura TFA, Medeiros ACD, Gomes APB, Aragã CFS. Compatibility Studies of Trioxsalen with Excipients by DSC, DTA, and FTIR. *J. Therm. Anal. Cal.*, 2014; 115: 2311-2318.
221. Rosasco MA, Bonafede SL, Faudone SN, Segall AI. Compatibility Study Between Tobramycin and Pharmaceutical Excipients Using Differential Scanning Calorimetry, FT-IR, DRX and HPLC. *J Therm. Anal. Cal.*, 2018; 134: 1929-1941.