WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 6, 1247-1292. Research Article ISSN 2277–7105

ACYCLOVIR-EXCIPIENT COMPATIBILITY STUDIES FOR GEL NOVEL DRUG DELIVERY SYSTEMS DEVELOPMENT

Mahmoud Mahyoob Alburyhi[1,4]*, Tawfeek A. A. Yahya[2], Abdalwali Ahmed Saif[1], Maged Alwan Noman[1,5], Nabila Alshoba[3] and Sami Ahmed Saeed[6]

[1]Professor Dr. of Pharmaceutics and Industrial Pharmacy, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[2]Professor Dr. of Medicinal Chemistry and Drug Design, Department of Medicinal Chemistry, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[3]Assistant Professor Dr. of Medicinal Chemistry and Drug Design, Department of Medicinal Chemistry, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[4]Department of Pharmacy, Faculty of Medical and Health Sciences, AlJeel AlJadeed University, Yemen.
[5]Department of Pharmacy, Faculty of Medical Sciences, Al-Yemenia University, Sana'a, Yemen.
[6]Assistant Professor Dr. of Pharmaceutics and Industrial Pharmacy, Sana'a, Yemen.

Article Received on 15 Feb. 2026,
Article Revised on 05 March 2026,
Article Published on 16 March 2026,

https://doi.org/10.5281/zenodo.19047133

***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.

How to cite this Article: Mahmoud Mahyoob Alburyhi[1,4]*, Tawfeek A. A. Yahya[2], Abdalwali Ahmed Saif[1], Maged Alwan Noman[1,5], Nabila Alshoba[3] and Sami Ahmed Saeed[6]. (2026). Acyclovir-Excipient Compatibility Studies For Gel Novel Drug Delivery Systems Development. World Journal of Pharmaceutical Research, 15(6), 1247–1292.

ABSTRACT

Oral herpes is a common, recurrent condition marked by painful mucosal lesions. Acyclovir is a guanosine antiviral drug and is one of the antiviral drugs most commonly used for treatment of herpes simplex virus infection, as well as herpes zoster and varicella zoster (chickenpox). Conventional topical treatments suffer from poor mucosal retention, low drug penetration, and limited patient compliance. Emulgel, combining the hydrophilic properties of gels with the biphasic structure of emulsions, offer enhanced solubility, stability, controlled release, and mucosal penetration. Additionally, Gels further offer ease of application, high spreadability, and good patient acceptability. Clove oil, a natural analgesic, anti-inflammatory, and antimicrobial agent, also improves taste, promoting better compliance. The main objective of the present study was to the preformulation studies were performed to know the development of formulation and evaluation of Acyclovir Hydrogel and Emulgel NDDS for topical

application. In the present study that the compatibility was assessed by, FTIR spectroscopy, and melting point apparatus, preformulation parameters. Results showed that physical mixtures of Acyclovir and various excipients such as Carbopol 974, Xanthan Gum, and HPC as gelling agents. Methylparaben and propylparaben served as preservatives, while propylene glycol, glycerin, Sucralose, Triethanolamine, Strawberry flavor, Clove oil and Tween were evaluated for preformulation studies parameters. It was concluded that the drug Acyclovir was found to be compatible with various excipients which were selected for the formulation development of the Acyclovir Hydrogel and Emulgel NDDS. Formulation scientist from his experience and knowledge have to significantly in the preformulation study stage and is an important factor in the ADDS (Advanced Drug Delivery Systems) product development process.

KEYWORDS: Acyclovir, NDDS, Compatibility, Excipients, Development, Preformulation, Hydrogel, Emulgel.

INTRODUCTION

Background on Herpes Simplex Virus Infection[1-9]

Herpesviruses are a family of DNA viruses found commonly in humans and animals. Nearly 100 herpesviruses have been at least partially characterized, and most animal species have been shown to be infected by at least one member of the family. The name, derived from the Greek herein, to creep, refers to the characteristic lesions caused by two common human herpesviruses: fever blisters caused by herpes simplex and varicella and shingles induced by herpes zoster. The known herpesviruses have a common virion. architecture and four significant biological properties: They encode a large variety of enzymes involved in nucleic acid metabolism, DNA synthesis and protein processing, synthesis of viral DNA and assembly of the capsid occurs in the nucleus of infected cells, the production of infectious viral progeny is usually accompanied by destruction of the infected cell and herpesviruses can remain latent and persist for life in their natural hosts.

Latent infection occurs in specific sets of cells that differ from one virus to another. The latent viral genomes usually take the form of circular episomes, and only a small subset of viral genes is expressed. Herpes simplex virus causes a wide variety of clinical manifestations. The clinical manifestation depends on: a) The age of patient b) Immune status of the host c) Previous immunity of the patient to autologous or heterologous viruses, d) antigenic type of the virus, and e) anatomical site of involvement. Typically, HSV-1 is

associated with orofacial infections (Cold sores) and encephalitis, while HSV-2 predominantly causes genital and neonatal infections. Primary infection with either virus is typically associated with systemic signs, prolonged duration, increased severity of illness and more complications.

Treatment of Herpes Simplex Virus Infection[10-15]

Although there is currently no vaccine or permanent cure for herpes simplex virus (HSV) infections, several pharmacological interventions are available to manage symptoms, reduce transmission, and suppress recurrence. Daily administration of antiviral medications such as Acyclovir, valacyclovir, or famciclovir has been shown to lessen the frequency and severity of symptomatic episodes and reduce viral shedding.

Acyclovir is a guanosine antiviral drug and is one of the antiviral drugs most commonly used for treatment of herpes simplex virus infection, as well as herpes zoster and varicella zoster (chickenpox).

Acyclovir: it is a synthetic acyclic purine nucleotide analog, which is most commonly used to treat HSV infection. Acyclovir is useful: To diminish shedding of viruses, to decrease rate of clinical recurrences and to suppress recurrent genital infections.

Oral therapy with Acyclovir is usually recommended for primary orolabial and genital HSV infections, which are non-life-threatening. Intravenous Acyclovir is recommended for life-threatening and serious HSV infection, such as encephalitis, infections in immunocompromised patients, and occasional severe orolabial or genital cases. Other antiviral agents, including famciclovir and valacyclovir, are effective in reducing both the transmission risk and the intensity of recurrent outbreaks. These medications are essential components of HSV management, especially in patients with frequent recurrences or severe disease. Supportive treatments, including analgesics such as paracetamol and topical anesthetics like lidocaine, can alleviate pain and discomfort associated with active lesions.

Pharmaceutical Research Paths[16-53]

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.

Compatibility Studies[54-120]

Preformulation is essentials of pharmaceutical science that utilizes biopharmaceutical principles in the determination of physicochemical properties of the drug substance. Prior to the development of any dosage form new drug, it is essential that certain fundamental physical and chemical properties of drug powder are determined. This information may dictate many of subsequent event and approaches in formulation development. The safety, efficacy, quality and stability of a formulation are major concepts of any API development process. In API development process, a detailed characterization of the API and other formulation components is usually carried out during the preformulation stage. Formulation scientist from his experience and knowledge have to significantly in the preformulation study stage and is an important factor in the ADDS (Advanced Drug Delivery Systems) product development process.

One of the objectives of this study is to development of drug delivery systems by building scientific pharmaceutical research information depend on formulation scientists to join the knowledge and experience as well as experimental and practical results of this study with regard to information in previous studies, and approved references. It was found to be that the most important concepts and basics of preformulation studies such as definitions, methods, conclusion, idea, and types of pharmaceutical analysis techniques using in evaluation of preformulation studies parameters, in this study that we focused on developing drug delivery systems and linking the formulation development to establish the basics of pharmaceutical research in studying the drug-excipient compatibility, dug with various excipients, which is important for the safety, effectiveness, quality, formulation, stability, bioavailability, and pharmacokinetics of the drug etc.

Determination of physical chemical properties of API substance with the goal of developing a new drug which is safe stable and efficacious, each API, has intrinsic chemical and physical properties that were considered prior to the development of pharmaceutical formulation, the purpose of preformulation study is to generate useful information for the formulator in the development of stable and bioavailable dosage form, inappropriate preformulation study results in poor stability of active ingredients increase the overall cost of development and increased development time, preformulation studies help to fortify the pharmaceutical scientific foundation of the guidance, provide regulatory relief and conserve resources in the drug development and evaluation process, enhance public safety standards, improve product

quality, promote the implementation of new technologies, aids policy development and regulatory decision making and after compiling all data it is transferred to the development pharmacist and for the day work on formulation of dosage form.

Preformulation Study Objectives: To establish the Physico-chemical parameters of a new API entity, determine its kinetics and stability, establish its compatibility with common excipients, it provides insights into how drug products should be processed and stored to ensure their quality, estimate problem may arise during formulation that is stability problem poor *in-vivo* dissolution, poor bioavailability, to interpret BCS classification of drugs and its significance and develop optimal drug delivery system.

Drug-Excipient Compatibility Study: The primary objective of this investigation was to identify a stable storage condition for API in solid state and identification of compatible excipients for its formulation. Incompatibilities are major concerns in formulation development. Selection of the proper excipient during preformulation studies is of prime importance.

Dosage Forms: DF contain API and pharmaceutical excipients, which are intended to generate an ideal formulation and manufacturability of pharmaceutical products, thereby enabling a much safer and more effective administration. Pharmaceutical excipients are ideally inactive and have no impact on the stability or therapeutic effect of the active ingredient. On the other hand, there are studies that have presented that some pharmaceutical excipients are just allegedly described as inactive ingredient. Some pharmaceutical excipients have the capacity to affect API, efficacy by affecting its pharmacokinetics. Excipients can affect the physical and chemical form of pharmaceuticals by several factors such as hydrogen bond interaction, polymorphic conversion, and others. Accordingly, drug-excipient compatibility should be conducted so as to determine any drug-excipient interactions that may obstruct the stability, bioavailability, and manufacturability of pharmaceutical dosage forms.

Importance of Drug-Excipient Compatibility

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 Acyclovir -excipient compatibility studies of the safety, efficacy, quality and stability of a formulation are major concepts of any API 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 Acyclovir Hydrogel and Emulgel NDDS for topical application.

MATERIALS AND METHODS

Acyclovir and all raw materials used in the preformulation and formulation including active pharmaceutical ingredients (APIs), excipients, and analytical reagents were obtained as a gift sample from (Global Pharma Pharmaceutical Industry Company - Yemen).

As shown in Table 1.

Table 1: List of Materials Used.

NO	Name of Materials
1	Acyclovir
2	Clove Oil
3	Carbopol
4	Xanthan Gum
5	Methylparaben
6	Propylparaben
7	Glycerin
8	Propylene Glycol
9	Tween 80
10	Sodium Lauryl Sulfate
11	Ethanol
12	Polyethylene Glycol 400
13	Polyethylene Glycol 6000
14	Sucralose
15	Flavor – Strawberry
16	Triethanolamine

Equipment

All equipment used are listed in

Table Error! No text of specified style in document.

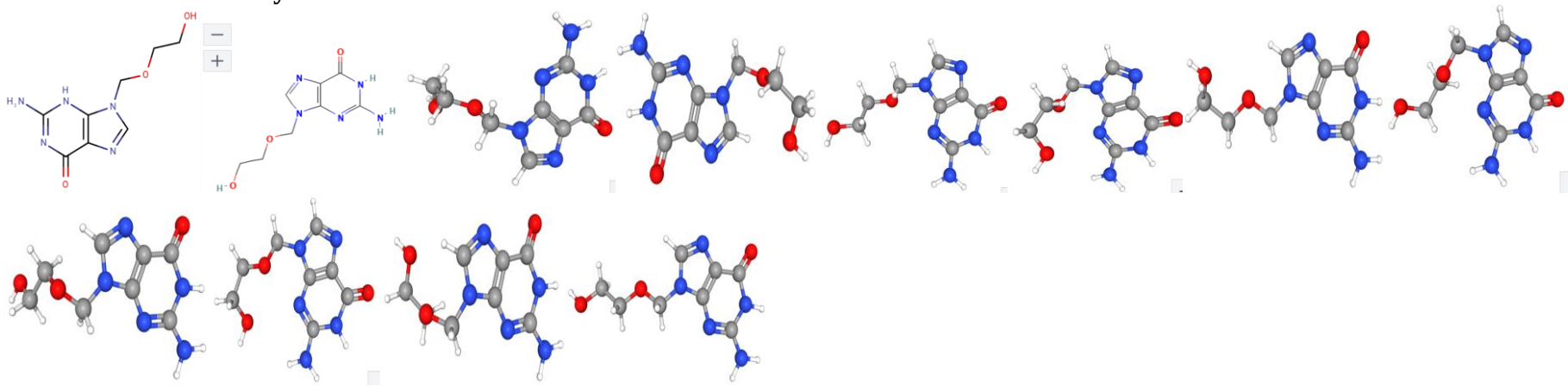
Table Error! No text of specified style in document.**: List of Instruments.**

NO	Instruments
1	Melting Point Apparatus
2	Chamber 40 °C
3	FTIR Spectrophotometer
4	UV-VIS Spectrophotometer
5	Sc Chemtech Ultrasonic Bath
6	pH Meter
7	Brookfield Viscometer
8	Magnetic Stirrer
9	Electronic Balance
10	Digital Thermostatic Water Bath

Evaluation of Drug-Excipient Compatibility Studies Methods.[88-186]

Table 3: Acyclovir Data.

Characterization of Acyclovir



Acyclovir Structure and 3D Conformer

Chemical Structure	2-amino-9-[(2-hydroxyethoxy) methyl]-6,9-dihydro-3H-purin-6-one	**Appearance**	White to off-white crystalline powder.
Chemical Formula	**$C_8H_{11}N_5O_3$**	**Drug Solubility**	Solubility: White, crystalline powder Slightly soluble in water (1.3 mg/ml at 25°C); very slightly soluble in ethanol (0.2 mg/ml); soluble in dilute aqueous solutions of alkali hydroxides and mineral acids; freely soluble in dimethyl sulfoxide. **Melting Point**: 256-257 °C.
Molecular Weight	225.20 g\mol	BCS	Class-III Drug
Drug Action and Use	Acyclovir is a guanosine antiviral drug and is one of the antiviral drugs most commonly used for treatment of herpes simplex virus infection, as well as herpes zoster and varicella zoster (chickenpox).		

<table>
<tr><td></td><td colspan="3">The ultimate effect of Acyclovir is the inhibition of viral DNA synthesis. Once transport into the cell, mono-phosphorylation is accomplished by a thymidine kinase that is encoded by the virus itself. The affinity of acyclovir for the viral thymidine kinase is about 200 times that of the corresponding mammalian enzyme. Hence, some selectivity is attained. Acyclovir monophosphate is converted to the diphosphate form by guanylate kinase. Acyclovir diphosphate is converted to Acyclovir triphosphate by nucleoside diphosphate kinase, pyruvate kinase, creatine kinase, phosphoglycerate kinase, succinyl-CoA synthetase, phosphoenolpyruvate carboxykinase and adenylosuccinate synthetase. Acyclovir triphosphate which is present in 40 to 100 times greater concentrations in HSV-infected than uninfected cells. Acyclovir triphosphate competes for endogenous deoxy guanosine triphosphate (dGTP); hence, Acyclovir triphosphate competitively inhibits viral DNA polymerases. The tri-phosphorylated drug is also incorporated into viral DNA, where it acts as a chain terminator. Because it has no 3 -hydroxyl group, no 3,5-phosphodiester bond can form. This mechanism is essentially a suicide inhibition because the terminated DNA template containing Acyclovir as a ligand binds to, and irreversibly inactivates DNA polymerase.</td></tr>
<tr><td colspan="4">Acyclovir Pharmacokinetics</td></tr>
<tr><td>Drug Absorption</td><td>The oral bioavailability of Acyclovir is 10 - 30% but decreases with increasing doses. dose-dependent due to saturable absorption mechanism, and the bioavailability of acyclovir is not affected by food.
Topical Absorption: Minimal systemic absorption from skin/mucosal surfaces. Acyclovir ointment is < 0.02-9.4% absorbed. Acyclovir buccal tablets and ophthalmic ointment are minimally absorbed. Acyclovir has a mean Tmax of 1.1 ± 0.4 hours, mean Cmax of 593.7 - 656.5ng/ml, and mean AUC of 2956.6 - 3102.5h/ng/ml.</td><td>Drug Distribution</td><td>Volume of Distribution:
The apparent volume of distribution of Acyclovir is reported to be 32.4 - 61.8 liter/1.73 sq m in adults and 28.8, 31.6, 42, or 51.2-53.6 liter/1.73 sq m in neonates up to 3 months of age, children 1-2 years; 2-7 years; or 7-12 years of age, respectively.
The volume of distribution of Acyclovir is 0.69 ± 0.19 L/kg.
Protein binding:
Acyclovir is 9-33% protein bound in plasma.</td></tr>
<tr><td>Drug Metabolism</td><td>Acyclovir is <15% oxidized to 9-carboxymethoxymethylguanine by alcohol dehydrogenase and aldehyde dehydrogenase and 1% 8-hydroxylated to 8-hydroxy-Acyclovir by aldehyde oxidase.</td><td>Drug Excretion</td><td>Route of Elimination:
The majority of Acyclovir (90-92%) is excreted through glomerular filtration and tubular secretion.is excreted in the urine as</td></tr>
</table>

			unchanged drug. < 2% of the drug is recovered in feces and < 0.1% is expired as CO_2. **Clearance:** The renal clearance of Acyclovir is 248ml/min/1.73m. The total clearance in neonates if 105-122ml/min/1.73m.
The Elimination Half-Life (T1/2)	Plasma elimination half-life varies from 2.5 - 3 hours depending on the creatinine clearance of the patient, prolonged in renal impairment). The plasma half-life of Acyclovir during hemodialysis is approximately 5 hours. The mean half-life in patients from 7 months to 7 years old is 2.6 hours.	**Availability**	Capsules: 200 mg. Tablets: 400 and 800 mg. Suspension: 200 mg/5 ml. Injection: 50 mg/ml. Powder for injection: 500 and 1000 mg. Ointment: 5%. Cream :5%.

Table 4: Pharmaceutical Excipients Data.

Nonproprietary Name	Synonyms	Functional Category	Incompatibilities
Carbomers	Acrypol; Acritamer; acrylic acid polymer; carbomera; Carbopol; carboxy polymethylene; polyacrylic acid; carboxyvinyl polymer; Pemulen; Tego Carbomer.	Bioadhesive material; controlled-release agent; emulsifying agent; emulsion stabilizer; rheology modifier; stabilizing agent; suspending agent; tablet binder.	Carbomers are discolored by resorcinol and are incompatible with phenol, cationic polymers, strong acids, and high levels of electrolytes. Trace levels of iron and other transition metals can catalytically degrade carbomer dispersions. Certain amino-functional actives form complexes with carbomer; often this can be prevented by adjusting the pH of the dispersion and/or the solubility parameter by using appropriate alcohols and polyols. Carbomers also form pH-dependent complexes with certain polymeric excipients. Adjustment of pH and/or solubility parameter can also work in this situation.
Clove Oil	Clove bud oil. Eugenia aromatica bud oil	Analgesic & Anesthetic:	Strong Oxidizing Agents: Can react violently.

	.Eugenia caryophyllata bud oil; Caryophylii floris aetheroleum; Clove volatile oil	Relieves toothaches (eugenol as a local anesthetic). Soothes muscle and joint pain. Antimicrobial: Combats bacteria, viruses, and fungi. Used in oral hygiene products. Anti-inflammatory: Reduces inflammation and swelling. Treats skin irritations. Antioxidant: Protects cells from free radical damage. Antiseptic: Disinfects minor wounds. Dental Applications: Alleviates dental pain, treats gingivitis, and disinfects cavities. Skincare: Addresses acne and purifies skin. Aromatherapy: Provides stimulating and invigorating effects.	iron: May cause discoloration. Zinc Oxide: Potential for chemical interaction. Certain Plastics/Rubber: Can degrade these materials. Highly Acidic/Basic Substances: May alter its composition
Xanthan Gum	Corn sugar gum; E415; Grindsted; Keldent; Keltrol; polysaccharide B-1459; Rhodicare S; Rhodigel; Vanzan NF; xanthani gummi; Xantural.	Gelling agent; stabilizing agent; suspending agent; sustained-release agent; viscosity-increasing agent.	Incompatible with cationic surfactants, polymers, and preservatives, often leading to precipitation, and at concentrations exceeding 15% w/v, anionic and amphoteric surfactants can also precipitate xanthan gum from solution. It is incompatible with oxidizing agents, some tablet film coatings, carboxymethylcellulose sodium, dried aluminum hydroxide gel, and certain active pharmaceutical ingredients.
Glycerin	Croderol; E422; glycerine; Glycon G-100; Kemstrene; Optim Pricerine; 1,2,3-propanetriol;	Antimicrobial preservative; emollient; humectant;	Glycerin may explode if mixed with strong oxidizing agents such as chromium trioxide, potassium chlorate,

	trihydroxypropane glycerol	plasticizer; solvent; sweetening agent; tonicity agent	or potassium permanganate. Black discoloration of glycerin occurs in the presence of light‹ or on contact with zinc oxide or basic bismuth nitrate. An iron contaminant in glycerin is responsible for the darkening in color of mixtures containing phenols, salicylates‹ and tannin. Glycerin forms a boric acid complex, glyceroboric acid, that is a stronger acid than boric acid.
Ethanol	Ethanolum (96 per cent), ethyl alcohol, ethyl hydroxide, grain alcohol, methyl carbinol.	Antimicrobial preservative, disinfectant, skin penetrant solvent.	In acidic conditions, ethanol solutions may react vigorously with oxidizing materials- alkali- aldehyde. Organic salts or acacia – Ethanol- aluminum.
Sodium Lauryl Sulfate (SLS)	Dodecyl sodium sulfate; Elfan 240; sodium dodecyl sulfate; sodium laurilsulfate; sodium monododecyl sulfate; sodium monolauryl sulfate; Texapon K12P	Anionic surfactant; detergent; emulsifying agent; skin penetration; tablet and capsule lubricant; wetting agent.	Reacts with cationic surfactants. Solutions of sodium lauryl sulfate (pH 9.5–10.0) are mildly corrosive to mild steel, copper, brass, bronze, and aluminum. Incompatible with some alkaloidal salts and precipitates with lead and potassium salts.
Sucralose	Splenda; sucralosa; sucralosum; SucraPlus; TGS; 10,40,60-trichlorogalactosucrose; 4,10,60-trichloro-4,10,60-trideoxy-galacto-sucrose	Sweetening agent	
Propylene glycol	12-dihydroxypropane, E1520, 2-hydroxypropanol;methylethyleneglycol, methyl glycol, propane-1,2diol, propylaglycolum.	Antimicrobial, preservative, disinfectant, humectant, plasticizer, solvent, stabilizing agent, water miscible cosolvent.	Propylene glycol is incompatible with oxidizing reagents such as potassium permanganate
Tween 80	Monolaurates, polyoxyethylene sorbitan, polysorbate	Emulsifying agent for the preparation of stable oil-in-water emulsions.	Incompatible with alkalis, heavy metal salts, phenols, tannic acid.
Saccharin	1,2-Benzisothiazolin-3-one 1,1-dioxide, sodium	Sweetening agent.	Saccharin can react with large molecules. Saccharin

Sodium	salt, Crystallose, E954, gendorf 450, sucaryl sodium	Saccharin can be used to mask some unpleasant taste characteristics or to enhance flavor systems. Its sweetening power is approximately 300–600 times that of sucrose.	sodium does not undergo Maillard browning
Triethanolamine	Tea, Tealan, triethylolamine, trihydroxytriethylamine, tris (hydroxyethyl)amine , trolaminum.	Alkalizing agent**,** emulsifying agent**,** pH adjuster.	Triethanolamine will react with mineral acids to form crystalline salts and esters. With the higher fatty acids- copper to form complex salts- with reagents such as thionyl chloride.
Methylparaben	Methyl ester of p-hydroxybenzoic acid, Methyl 4-hydroxybenzoate, Nipagin M., Methyl parahydroxybenzoate, Methyl parahydroxybenzoic acid, Methyl chemosept, MPB, Metoxyguard, Tegosept M, Methyl-p-hydroxybenzoate.	Preservative.	Methyl paraben can undergo hydrolysis under acidic conditions, resulting in the formation of p-hydroxybenzoic acid. Methyl paraben may react with oxidizing agents, such as hydrogen peroxide, and lose its effectiveness as a preservative. Methyl paraben can form complexes with certain metal ions, such as aluminum and iron.
Propyl Paraben	Propyl p-hydroxybenzoate, Propylparaben, E216 (E-number used in food additives), Propyl ester of p-hydroxybenzoic acid	preservatives.	Magnesium aluminum silicate, magnesium trisilicate, yellow iron oxide, and ultra- marine blue have also been reported to absorb propylparaben.
Purified water	Filtered water, Distilled water, Deionized water, Purified H2O, Clear water, Pure water, clean water, Pristine water, Crystal-clear water, Treated water	solvent	In pharmaceutical formulations, water can react with drugs and other excipients that are susceptible to hydrolysis (decomposition in the presence of water or moisture) at ambient and elevated temperatures. Water can react violently with alkali metals and rapidly with alkaline metals and their oxides, such as calcium oxide and magnesium oxide. Water also reacts with anhydrous salts to form hydrates of various compositions, and with certain organic materials and calcium carbide.

According to Acyclovir and excipients data as shown in Tables 3 and 4, it was selected that the different excipients to preformulation study with Acyclovir in the present study,

Drug Identification Tests

Melting Point

Melting point of the Acyclovir was determined by capillary method, one sided closed capillary filled with drug and put into the Melting Point Apparatus. Temperature was noted at which solid drug changed into liquid.

UV-Vis Spectrophotometer Analysis of Acyclovir

A standard solution of Acyclovir was prepared by diluting the stock in purified water to a final concentration of 15 µg/ml. Spectra were acquired on a double‑beam UV–Vis spectrophotometer using 1 cm path‑length quartz cuvettes, scanning from 200 to 800 nm. Baseline correction was performed with purified water to eliminate solvent absorbance. The result was then compared to the reported λmax range of 252–254 nm in aqueous media.

Calibration Curve of Acyclovir

15 mg of Acyclovir was weighed accurately and dissolved in 100 ml of purified water in a 100 ml volumetric flask to obtain a stock solution (150 µg/ml). Aliquots of 10 ml were taken from the stock solution and transferred to a 50 ml volumetric flask, then the volume was made up to 50 ml with purified water to obtain a concentration of 30 µg/ml. From this solution, 25 ml aliquots were successively transferred to 50 ml volumetric flasks and diluted to volume with purified water to prepare a series of standard solutions with concentrations of 15 µg/ml, 7.5 µg/mL, 3.75 µg/ml, and 1.875 µg/ml. The absorbance of these solutions was measured at 252nm against a blank of purified water. The calibration curve was plotted between concentration and absorbance.

Pre-Formulation Study

A stage of development during which the physicochemical properties of the drug substance are characterized and established. A complete knowledge of the relevant therapeutic and physicochemical properties of the drug enables determination of its proper formulation and delivery method. Preformulation study is to develop the elegant (stable, effective, and safe) dosage form by establishing kinetic rate profile, compatibility with the other ingredients and establish physico-chemical parameter of new drug substance.

Organoleptic Properties

The organoleptic properties of the active pharmaceutical ingredient (API) were evaluated by assessing color, odor, and using standardized sensory methods: Color: A small quantity of Acyclovir was placed on butter paper and examined under well-illuminated conditions to determine its color characteristics. Odor: A minimal amount of the sample was used to assess its odor through direct sensory evaluation.

Solubility Study

Solubility is a critical physicochemical parameter that directly influences drug absorption, bioavailability, and therapeutic efficacy. Poor aqueous solubility can significantly hinder formulation development, leading to suboptimal drug delivery and potential clinical failure.

An initial solubility screening of Acyclovir was carried out at room temperature (25°C) using various aqueous and non-aqueous solvent systems. This essential preformulation analysis provides critical data for optimal solvent and excipient selection in formulation development.

The aqueous solubility evaluation involved dispersing 100 mg of Acyclovir in 1 ml aliquots of different media: Purified water, 0.1 N hydrochloric acid (pH 1.2), Acetate buffer solution (pH 4.5) and Phosphate buffer (pH 6.8). All buffer solutions were prepared in compliance with USP standards. The mixtures were gently agitated for one minute followed by 10 minutes of sonication. For samples where complete dissolution was not achieved, additional solvent was added in increments to reach final volumes of 5ml, 10 ml, 20 ml, 30 ml, 40ml, 50 mL, and up to 100ml. The solubility profile was categorized according to the minimum solvent volume needed for complete visual dissolution.

For organic solvent systems, 100 mg of Acyclovir was dispersed in: glycerin, propylene glycol (PG), 1% w/v tween 80 solution, 1% w/v sodium lauryl sulfate (SLS) solution, PG/tween 80 binary mixture (1:1 ratio) and PG/SLS combination (1:1 ratio). All non-aqueous samples were brought to a final volume of 10 ml. Following manual stirring and 15 minutes of sonication, each preparation was visually inspected for uniformity of dispersion, phase stability, and foaming characteristics. This comprehensive solubility assessment establishes fundamental data for subsequent formulation optimization work as shown in Table 5.

Table 5: Solubility Specification of Drugs.

Descriptive Term	Parts of Solvent Required for 1 Part of Solute:
Very Soluble	Less than 1
Freely Soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly Soluble	From 30 to 100
Slightly Soluble	From 100 to 1000
Very Slightly Soluble	From 1000 to 10000
Practically Insoluble, or Insoluble	Greater than or equal to 10,000.

Drug and Excipients Compatibility Study

FTIR Spectroscopy Study

IR study was aimed to study the compatibility of excipients with Acyclovir in room condition. Each excipient was mixed with Acyclovir in equal amounts, then from each sample a small amount was taken (approx 1:1 %) and mixed with about 100 mg of potassium bromide. The KBr- sample mixtures were grinded separately for each sample using agate mortar and pestle. The grinded powders were compressed into discs under pressure of about 10000 pounds per square inch. The tablets were mounted in IR compartment and analyzed. The infrared spectra of the drug - excipient mixtures were recorded over a wave number of 4000 cm^{-1} to 500 cm^{-1}. On analysis of the IR spectra of the reference spectra given in British Pharmacopoeia and pure drug, no major differences were observed in the characteristic absorption peak pattern as shown in Table 6.

Table 6: The Drug and Excipients Compatibility Studies.

Sample Code	Drug with Excipients	Ratio (Drug: Excipient)
1	Acyclovir	1
2	Acyclovir+ Clove oil	1:1
3	Acyclovir + HPC	1:1
4	Acyclovir + PEG	1:1
5	Acyclovir + Tween 80	1:1
6	Acyclovir + NaOH	1:1
7	Acyclovir + Ethanol	1:1
8	Acyclovir + Triethanolamine	1:1
9	Acyclovir + SLS	1:1
10	Acyclovir + Sucralose	1:1
11	Acyclovir + Sodium Saccharin	1:1
12	Acyclovir + Glycerin	1:1
13	Acyclovir + Xanthan Gum	1:1
14	Acyclovir + Carbopol	1:1
15	Acyclovir + Sodium Methyl Parapan	1:1
16	Acyclovir + Propylene Glycol	1:1

RESULTS AND DISCUSSION

Drug Identification Tests

Organoleptic properties

The organoleptic properties of the active pharmaceutical ingredient (API) were evaluated by assessing color, odor, and using standardized sensory methods. Results are presented for Acyclovir in the Table 7.

Table 7: Organoleptic Properties of Acyclovir.

Observations	Specifications	Tests
White powder	White to off -white powder	Appearance
Odorless	Odorless	Odor

Characterization of Acyclovir by UV Spectroscopy

UV Scanning of Acyclovir in Purified Water

The identity of Acyclovir was confirmed by recording their UV–Vis absorption spectra in purified water. A 15 µg/mL Acyclovir solution was scanned over a wavelength range of 200–800 nm using a double-beam spectrophotometer with 1 cm quartz cuvettes as shown in Figure 1. Acyclovir exhibited a distinct absorption maximum (λmax) at 252.6 nm, which is consistent with the reported λmax range of 252–254 nm for Acyclovir in aqueous media.

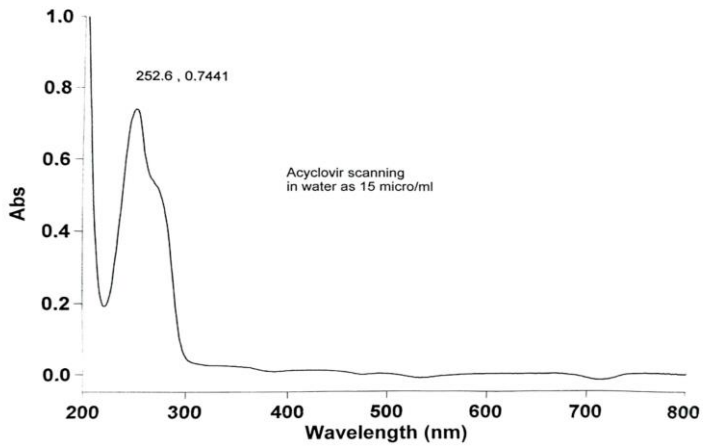


Fig. 1: Wavelength of Acyclovir in UV Spectrophotometer.

Calibration curve of Acyclovir in Purified Water

Acyclovir exhibited a distinct absorption maximum (λmax) at 252.6 nm, which is consistent with the reported λmax range of 252–254 nm for Acyclovir in aqueous media. The calibration curve was plotted between concentration and absorbance as shown in Table 8, and Figure 2.

Table 8: Calibration Curve Results of Acyclovir in Purified Water.

NO	Concentration	Absorbance	SD
1	1.875	0.1173	0.0001
2	3.75	0.237	0.0002
3	7.5	0.4463	0.0002
4	15	0.8895	0.0006
5	30	1.7891	0.0013

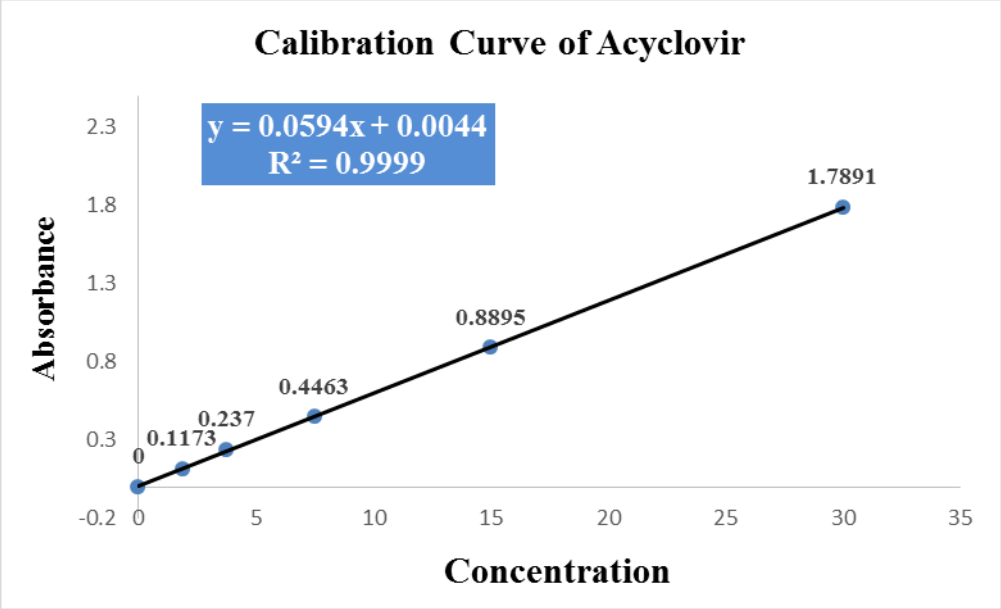


Fig. 2: Calibration Curve of Acyclovir in Purified Water.

Solubility Study

The dissolution characteristics of Acyclovir were systematically investigated in multiple solvent systems at ambient temperature (25±1°C). The study employed a dropwise addition method with continuous agitation to determine saturation points, with solubility categorization according to USP standards, as shown in **Error! Reference source not found.**.

Table 9: Solubility Study Determination of Acyclovir.

NO	Solubility Media	Results
1	Purified Water	Sparingly Soluble
2	Dilute hydrochloric acid (HCl) pH 1.2	Soluble
3	Buffer solution pH 4.5	Slightly Soluble
4	Buffer solution pH 6.8	Soluble
5	Non-aqueous media	Insoluble

Melting Point Determination of Acyclovir

Melting point of pure Acyclovir was determined by open capillary method. The capillary tube

was closed at one end by fusion and was filled with Acyclovir 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 d melting was recorded. The melting point range of Acyclovir was identical to reference melting point stated in MP (256.5–257.5°C). The sample started to melt at 256°C, and turned into liquid at 257°C, indicating that the sample used is pure. That reading has stated in melting point tester.as shown in Table 10.

Table 10: Results of Melting Point of Acyclovir.

Test	Temp Rang Analyzed (Melting)	Results
Test I Acyclovir	(256.5–257.5°C)	257°C
Test II Acyclovir	(256.5–257.5°C)	257°C

Excipient and Drug Compatibility Study

Characterization of Acyclovir by FTIR

FTIR spectrum studies indicated that major functional groups present in Acyclovir show characteristic peaks in IR spectrum. Figures (3) to (18) show peaks observed at different wave numbers and the functional group associated with these peaks for drug and drug with different excipients. The major peaks are identical to functional group of Acyclovir. Hence, it was confirmed that there was compatibility between drug and various excipients, thus conforming that no interaction of drug occurred with the components of the formulation excipients.

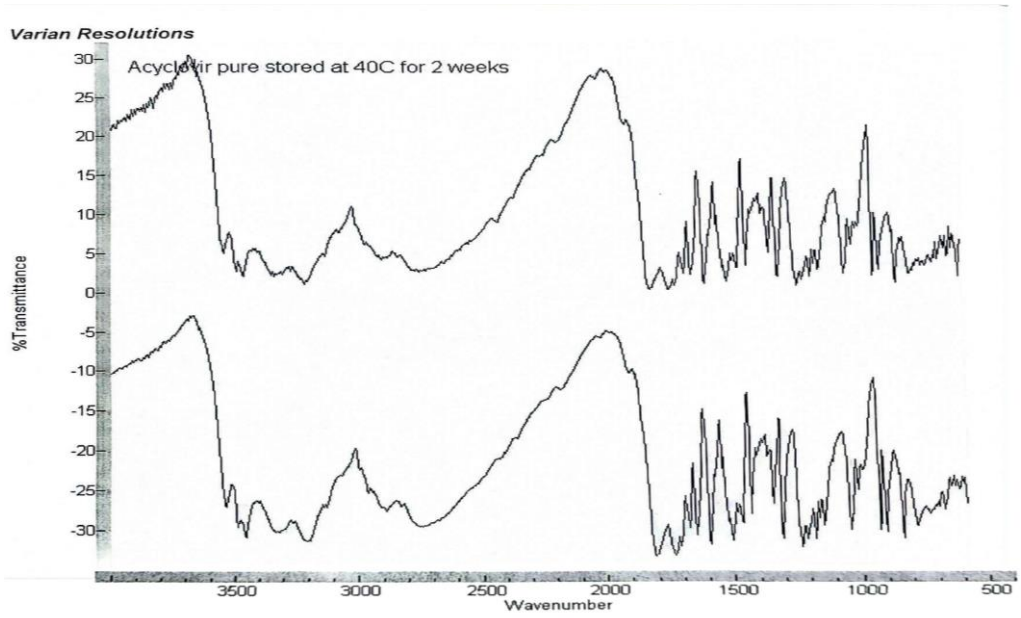


Fig. 3: FTIR Spectra of Pure Acyclovir STD Fresh and Stored.

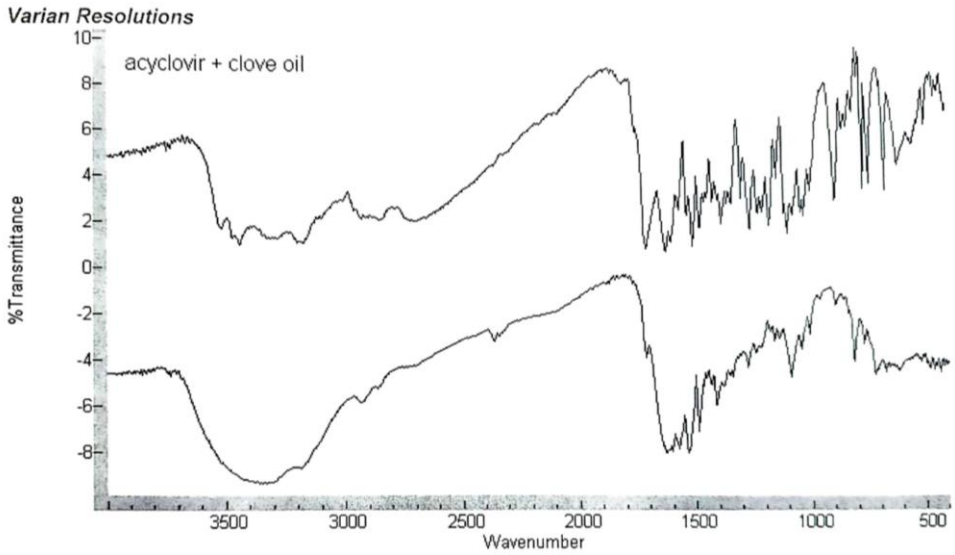


Fig. 4: FTIR Spectra of Acyclovir with Clove Oil.

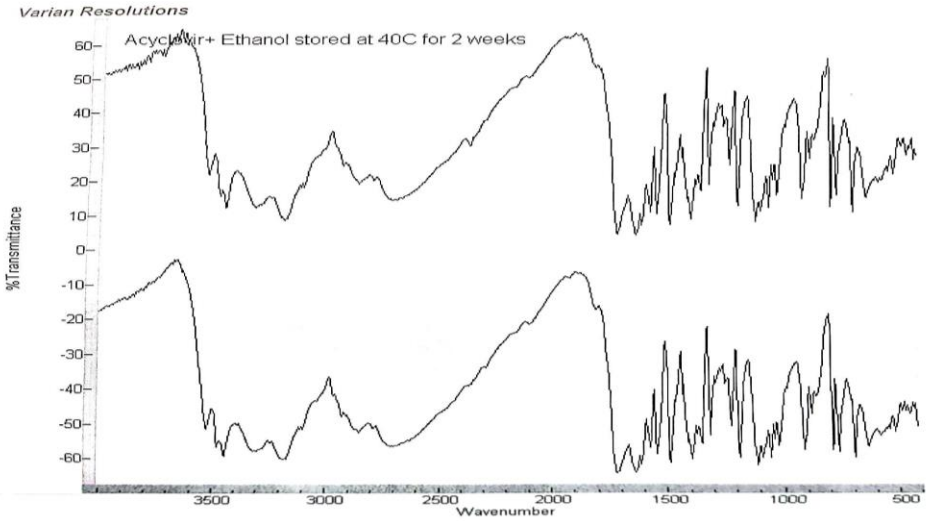


Fig. 5: FTIR Spectra of Acyclovir with Polyethylene Glycol (PEG).

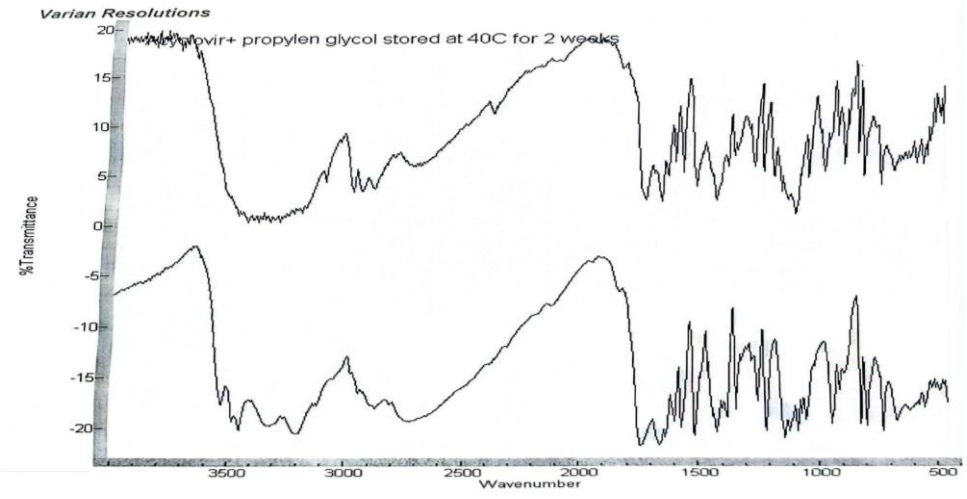


Fig. 6: FTIR Spectra of Acyclovir with Propylene Glycol (PG).

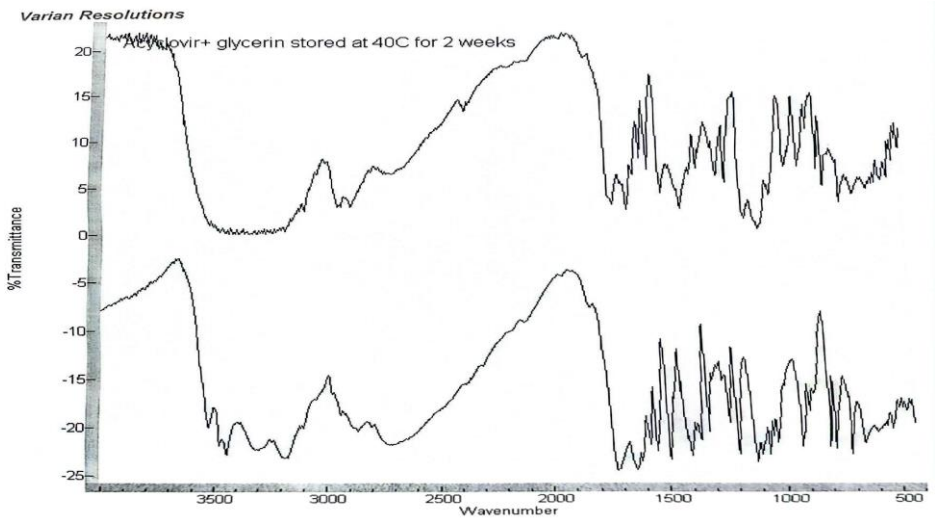


Fig. 7: FTIR Spectra of Acyclovir with Ethanol.

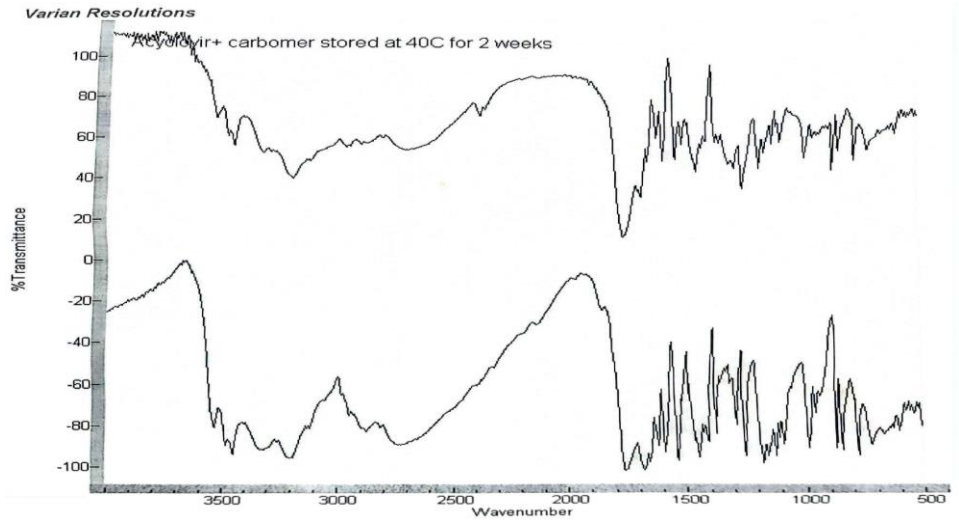


Fig. 8: FTIR Spectra of Acyclovir with Glycerin.

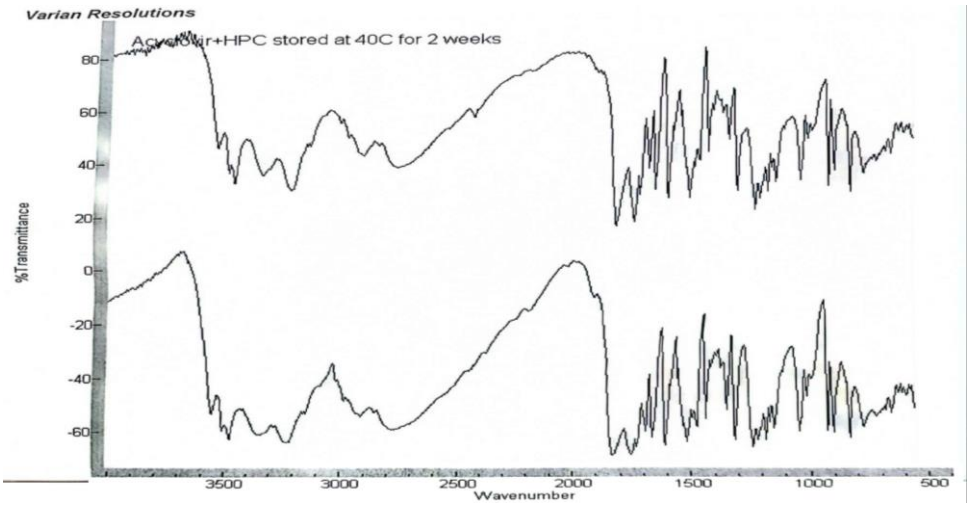


Fig. 9: FTIR Spectra of Acyclovir with HPC.

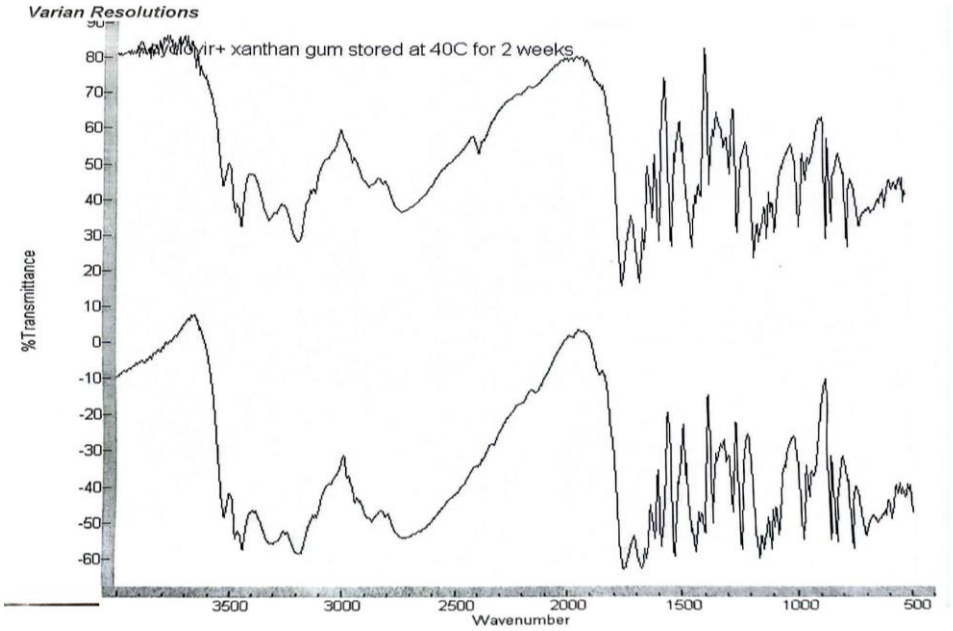


Fig. 10: FTIR Spectra of Acyclovir with Carbomer.

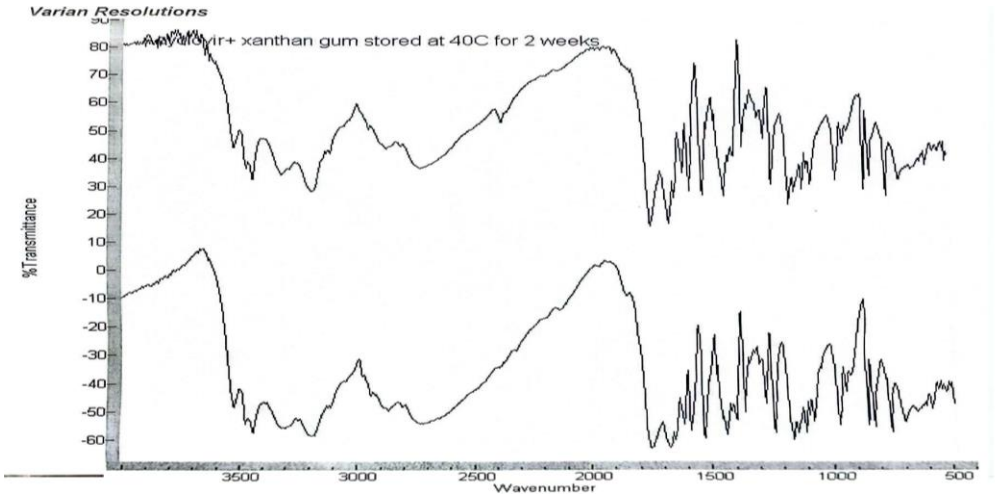


Fig. 11: FTIR Spectra of Acyclovir with Xanthan Gum.

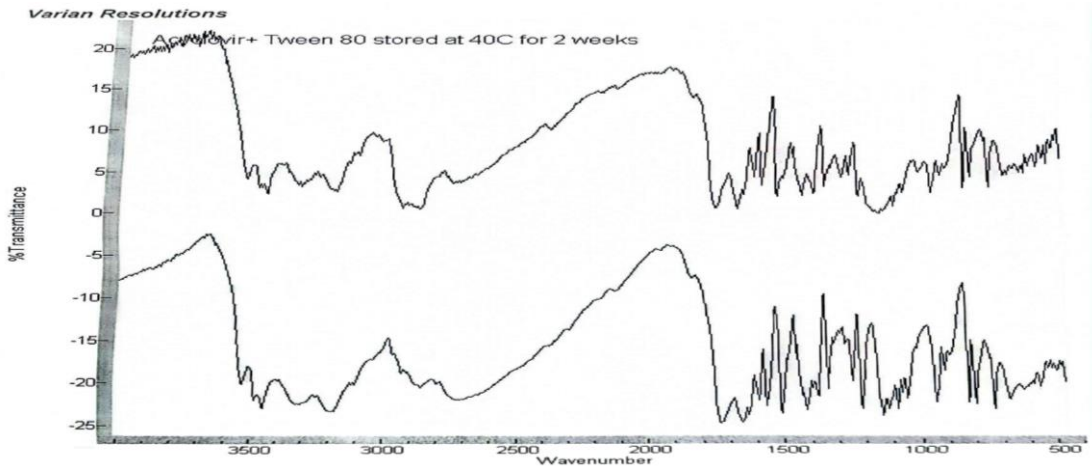


Fig. 12: FTIR Spectra of Acyclovir with Tween 80.

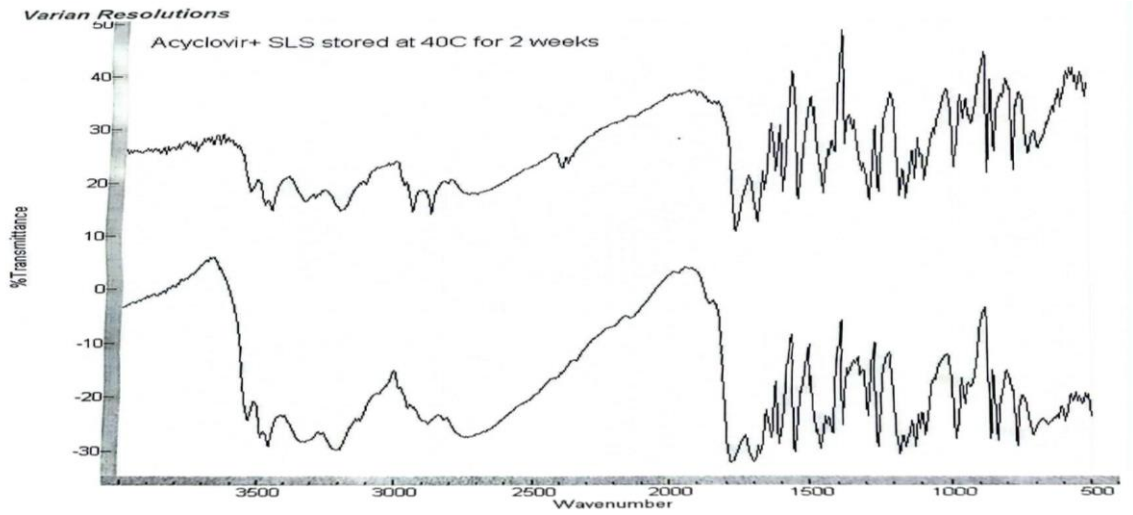


Fig. 13: FTIR Spectra of Acyclovir with Sodium Lauryl Sulfate.

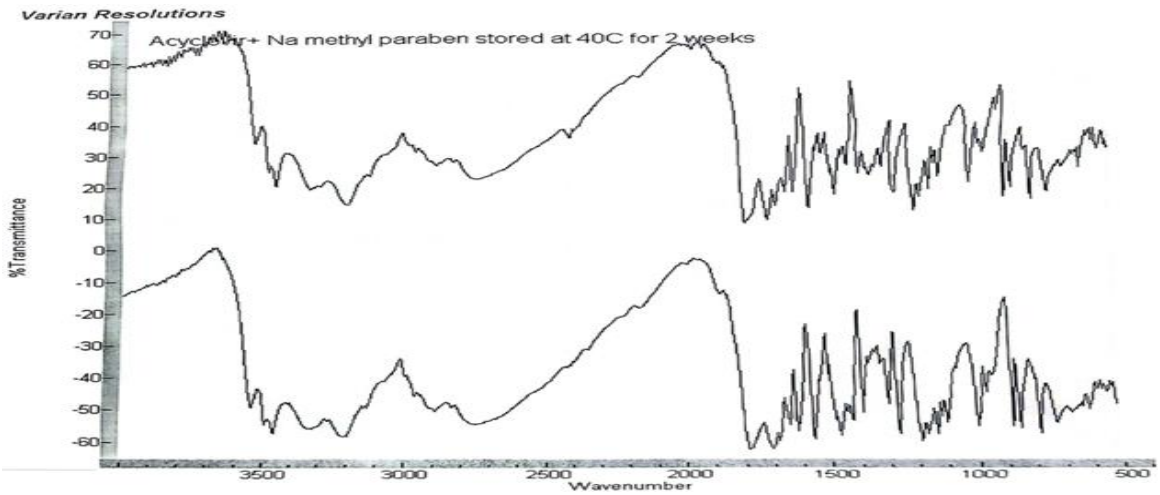


Fig. 14: FTIR Spectra of Acyclovir with Sodium Methylparaben.

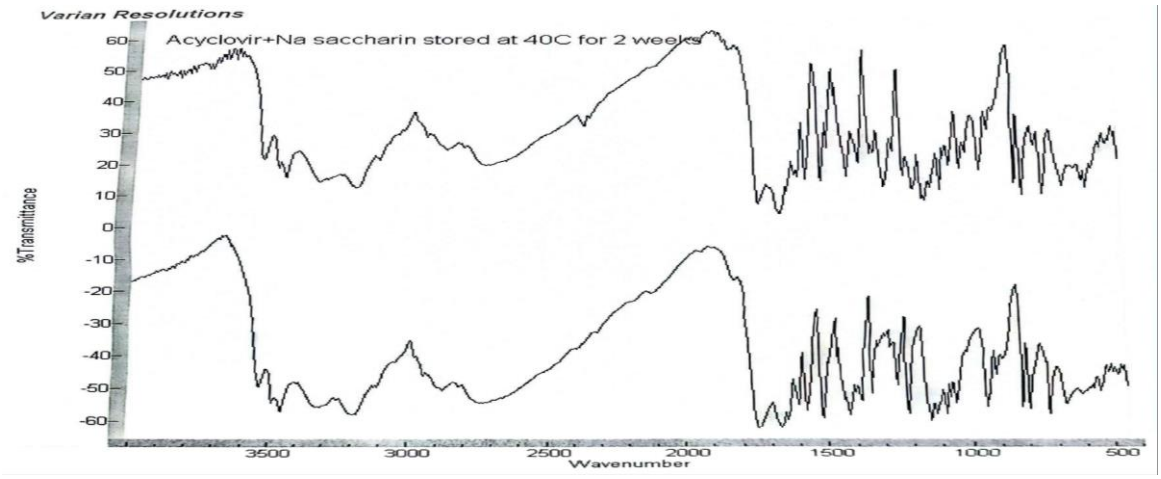


Fig. 15: FTIR Spectra of Acyclovir with Sodium Saccharin.

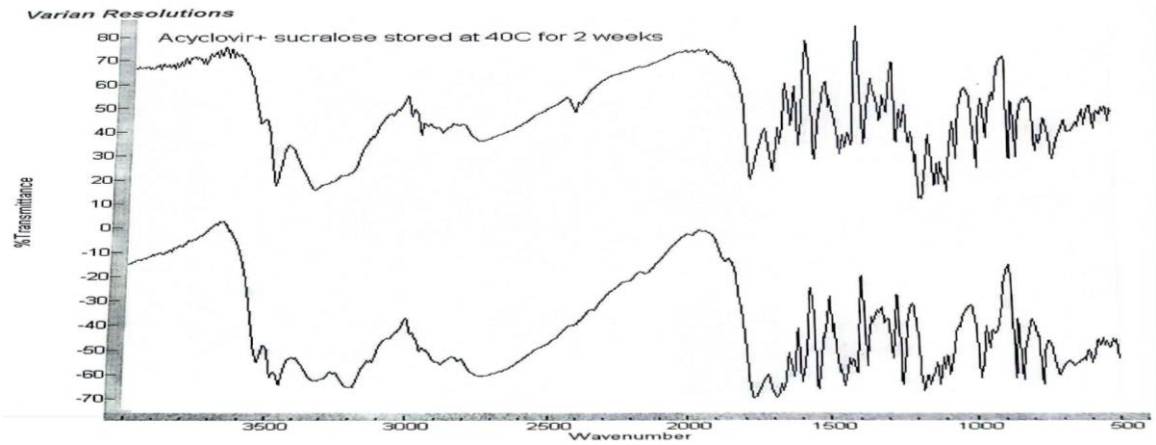


Fig. 16: FTIR Spectra of Acyclovir with Sucralose.

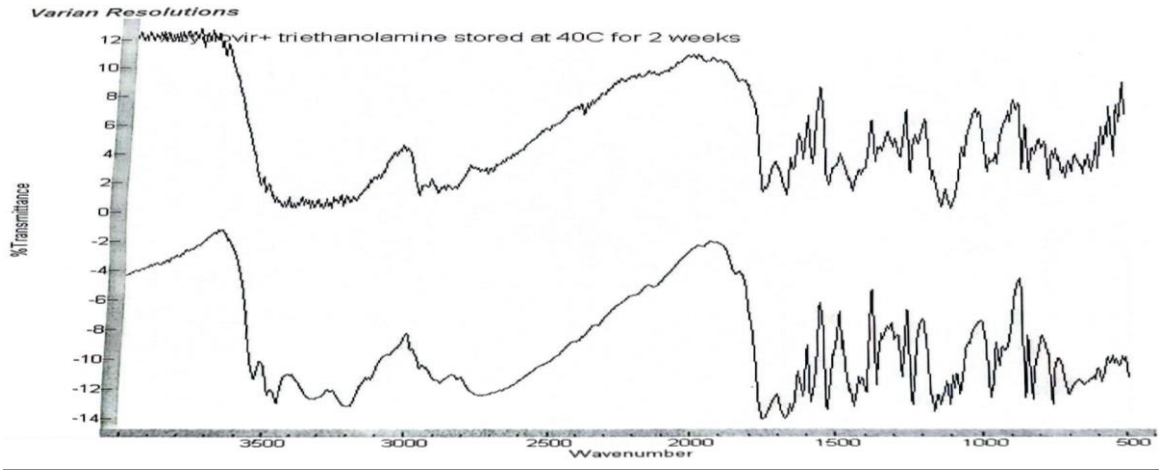


Fig. 17: FTIR Spectra of Acyclovir with Triethanolamine.

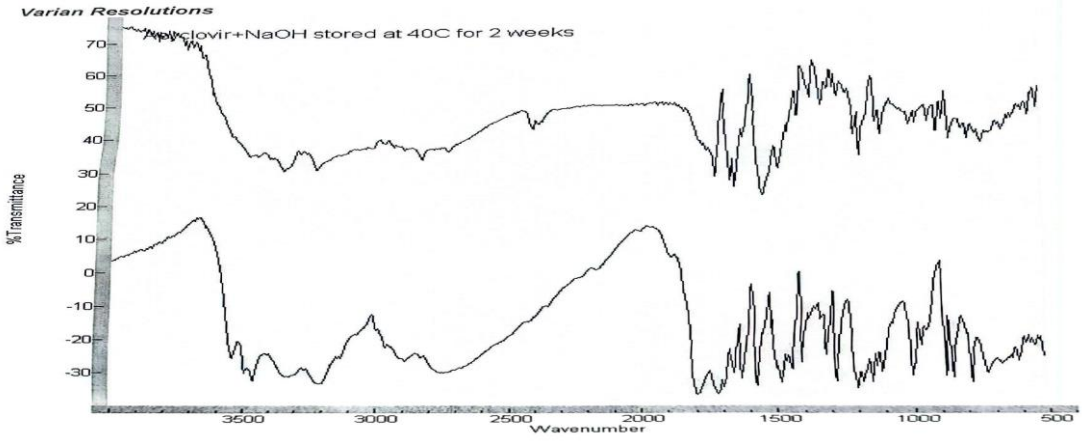


Fig. 18: FTIR Spectra of Acyclovir with Sodium Hydroxide.

DISCUSSION

The FTIR spectrum of pure Acyclovir was obtained to establish characteristic absorption regions for subsequent drug–excipient compatibility assessments (Figure 3). Spectra of both

freshly prepared Acyclovir and the sample subjected to accelerated storage conditions (40 ± 2 °C, 75 % RH for 14 days) were recorded and found to be superimposable, confirming chemical stability under the applied stress conditions. The absorption regions exhibited in the spectrum of fresh Acyclovir as shown in Figure 3, are presented in
Table 1.

Table 11: Characteristic FTIR Absorption Regions of Pure Acyclovir.

Wavenumber (cm^{-1})	Assignment
3500–3100 (broad)	A prominent, broad absorption band due to the overlapping O–H and N–H stretching vibrations from the side chain and purine ring.
3000 - 2800	Attributed to aliphatic C–H stretching vibrations from the ethyl group ($–CH_2CH_3$) within the side chain.
1800 – 1650 (intense)	This range contains the sharp, intense C=O (carbonyl) stretching vibration, the most specific reporter peak for the Acyclovir molecule.
1650 – 1500	A diagnostic region containing multiple sharp peaks from the C=N and C=C skeletal stretching of purine ring, and the N-H bending vibration.
1300–1000	This part of the fingerprint region is dominated by C–N and C–O single bond stretching from both the purine ring and the acyclic chain.

No new absorption bands, significant shifts in wavenumber (exceeding ±3 cm^{-1}), or notable changes in peak intensity were observed in the spectrum of the stored sample (**Error! Reference source not found.**), confirming the chemical integrity of Acyclovir under the applied accelerated storage conditions. These results validate the stability of Acyclovir and its suitability for use in subsequent drug–excipient interaction studies.

The Acyclovir–clove oil mixture (**Error! Reference source not found.**) exhibited a pronounced broadening and deepening of the 3500–3100 cm^{-1} envelope, with a concomitant loss of sharpness in all characteristic drug peaks. Despite this physical masking, no new absorption bands appeared, nor did any diagnostic peaks shift by more than 5 cm^{-1}. The C=O stretch at 1709 cm^{-1} and the C=N/C=C vibrations at 1631–1484 cm^{-1} remained intact, confirming that the interaction is purely physical and that clove oil is fully compatible with Acyclovir.

In the polyol group and ethanol, each of polyethylene glycol (PEG; **Error! Reference source not found.**), propylene glycol (**Error! Reference source not found.**), ethanol (**Error! Reference source not found.**), and glycerin (**Error! Reference source not found.**)

produced a broad O–H absorption envelope in the 3500–3100 cm^{-1} region that overlapped Acyclovir's N–H, O-H stretches. Despite this high-wavenumber masking, the diagnostic C=O band at 1800–1650 cm^{-1} and the C=N/C=C skeletal vibrations at 1650–1500 cm^{-1}) remained completely unshifted and unchanged in intensity in all four mixtures, confirming that only peaks overlap occurred and that each polyol is fully compatible with Acyclovir.

Similarly, the polymeric and gelling agents-hydroxypropyl cellulose (HPC; **Error! Reference source not found.**), Carbomer (**Error! Reference source not found.**), and xanthan gum (**Error! Reference source not found.**) -each showed only a broadening of the 3500–3100 cm^{-1} band due to overlapping –OH and N–H vibrations. In every case, the carbonyl stretches and the C=N/C=C skeletal bands retained their original sharpness and positions, demonstrating no evidence of chemical interaction and indicating full compatibility.

In the surfactant category, both the Acyclovir–polysorbate 80 (Tween 80; **Error! Reference source not found.**) and Acyclovir–sodium lauryl sulfate (SLS; **Error! Reference source not found.**) mixtures. The core diagnostic peaks of Acyclovir-the C=O stretch and the C=N/C=C skeletal vibrations between remained entirely unchanged in position and intensity in both mixtures. In SLS-ACV mixture notable increase in the intensity of the aliphatic C-H stretching peaks (2950–2850 cm^{-1}) was observed, an additive effect from the SLS alkyl chain. Additionally, a subtle alteration in the shape and relative intensities of Acyclovir's N-H stretching peaks (3500–3100 cm^{-1}) was noted, suggesting a minor physical interaction through hydrogen bonding between the drug's N-H groups and the electronegative oxygen atoms of the SLS sulfate group. No new absorption bands or significant spectral shifts were observed, confirming that Tween 80 is compatible and SLS interact only physically with Acyclovir, indicating full compatibility under the conditions tested.

Among the small-molecule additives, sodium methylparaben (**Error! Reference source not found.**), sodium saccharin (**Error! Reference source not found.**), sucralose (**Error! Reference source not found.**), and triethanolamine (TEA;
) each produced simple additive spectra. None of these mixtures generated new absorption bands nor shifted the characteristic C=O and C=N/C=C vibrations, corroborating their physicochemical compatibility with Acyclovir.

By contrast, the Acyclovir–sodium hydroxide (NaOH; **Error! Reference source not found.**)

mixture underwent profound spectral changes: the 1800–1650 cm^{-1} C=O band completely disappeared, crystalline fingerprint peaks were altered, with the loss of many sharp crystalline peaks and the appearance of new bands. and the N–H envelope was replaced by a broad undefined band. These alterations are hallmarks of deprotonation and sodium-salt formation, confirming a true chemical reaction and indicating that NaOH is incompatible with Acyclovir in solid formulations.

The pre-formulation studies confirmed the identity and purity of the active drugs. The measured melting point of Acyclovir (256–257 °C) matched the USP reference range, and UV–Vis spectra showed characteristic λ-max values for Acyclovir. Importantly, FTIR analysis showed that Acyclovir retained its diagnostic bands under stress and in mixtures with formulation excipients. For example, Acyclovir blended with clove oil or polyols produced only broadening of O–H bands, with the C=O and C=N stretches unshifted. Likewise, gelling polymers (HPC, carbomer, xanthan) and surfactants (Tween 80, SLS) exhibited only overlapping peaks and no new absorption bands. These findings demonstrate full physicochemical compatibility of acyclovir with all gel and emulsion components. In other words, none of the excipients caused chemical degradation or new interactions with the drug.

CONCLUSION

The compatibility studies of physical mixtures of Acyclovir with different used excipients such as Carbopol 974, Xanthan Gum, and HPC as gelling agents. Methylparaben and propylparaben served as preservatives, while propylene glycol, glycerin, Sucralose, Triethanolamine, Strawberry flavor, Clove oil and Tween were evaluated for preformulation studies parameters were investigated by FTIR it was detected that there was no variation or minor deviation in the characteristic peaks in FTIR spectroscopy. It was concluded that the drug Acyclovir was found to be compatible with various excipients which were selected for the formulation development of the Acyclovir Hydrogel and Emulgel NDDS. Formulation scientist from his experience and knowledge have to significantly in the preformulation study stage and is an important factor in the ADDS (Advanced Drug Delivery Systems) product development process.

ACKNOWLEDGEMENT

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

REFERENCES

1. Chayavichitsilp P, JV Buckwalter, AC Krakowski, SF Friedlander. Herpes simplex. Pediatrics in review, 2009; 30(4): 119-130.
2. Howley PM, DM Knipe, LW Enquist, Fields Virology: Fundamentals. Lippincott Williams & Wilkins, 2023.
3. Whitley, R., Herpesviruses, in Medical Microbiology, S. Baron, Editor. University of Texas Medical Branch at Galveston Galveston (TX), 1996.
4. Kramer T, LW Enquist. Directional spread of alphaherpesviruses in the nervous system. Viruses, 2013; 5(2): 678-707.
5. Balasubramaniam, R., A.S. Kuperstein, and E.T. Stoopler, Update on oral herpes virus infections. Dental Clinics., 2014. 58(2): 265-280.
6. Centers for Disease, C. and Prevention. Genital Herpes –CDC Fact Sheet, 2023; Available from: https://www.cdc.gov/std/herpes/STDFact-Herpes-detailed.htm.
7. James, S.H. and D.W. Kimberlin, Neonatal herpes simplex virus infection. Infectious Disease Clinics, 2015; 29(3): 391-400.
8. Gupta R, T Warren, A Wald. Genital herpes. The Lancet, 2007; 370(9605): 2127-2137.
9. Wald A, L Corey. Persistence in the population: epidemiology, transmission, in Human Herpesviruses: Biology, Therapy, and Immunoprophylaxis, A. Arvin, et al., Editors. Cambridge University Press Copyright © Cambridge University Press 2007.
10. Leone P, Reducing the risk of transmitting genital herpes: advances in understanding and therapy. Current medical research and opinion, 2005. 21(10): 1577-1582.
11. World Health, O. Herpes simplex virus – Fact Sheet. Available from: https://www.who.int/news-room/fact-sheets/detail/herpes-simplex-virus, 2024.
12. O'Brien JJ, DM Campoli-Richards,. Acyclovir: an updated review of its antiviral activity, pharmacokinetic properties and therapeutic efficacy. Drugs, 1989; 37: 233-309.
13. Elad S, Y Zadik, I Hewson, A Hovan, MEP Correa, R Logan, LS Elting, FK Spijkervet, MT Brennan, OC SG. Viral Infections Section, Multinational Association of Supportive Care in Cancer /International Society of Oral Oncology, A systematic review of viral infections associated with oral involvement in cancer patients: a spotlight on Herpesviridea. Supportive care in cancer, 2010; 18: 993-1006.
14. FDA, U.S.F.a.D.A. Zovirax (acyclovir) prescribing information. 2022; Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/018828s030%2C020089s019%2C019909s020lbl.pdf.

15. Brunton L, B Knollmann. Goodman and Gilman's The Pharmacological Basis of Therapeutics, 14th Edition. McGraw Hill LLC. 2022.
16. 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.
17. 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.
18. 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.
19. Saif AA, Alburyhi MM, Noman MA, Almaktari 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.
20. Al-Ghorafi MA, Alburyhi MM. Evaluation and Formulation of Antifungal Activity of Dragon Blood Extract and Inorganic Salts on Dermatophytosis and Candidiasis. European Journal of Pharmaceutical and Medical Research., 2024; 11(1): 09-17.
21. Almamari A, Alburyhi MM, Alheggami MA, Alhag S. Identify and Sensitivity to Antifungal Drugs of Candida Species Causing Vaginitis Isolated from Vulvovaginal Infected Patients in Sana'a City. Der Pharma Chemica., 2014; 6(1): 336-342.
22. 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.
23. Alburyhi MM, Moharram BA. Formulation and Evaluation of Jatropha Variegata 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.
24. 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.
25. 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.

26. Alburyhi MM, Moharram BA. Formulation and Evaluation of Aloe Inermis Extract for Wound Healing Activity as Antibacterial Cream Novel Drug Delivery Systems. European Journal of Pharmaceutical and Medical Research., 2025; 12(10): 297-308.
27. 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.
28. 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.
29. Al-Ghani AM, Alkhawlani 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.
30. Al-Samawi HM, El-Shaibany A, Abdelkhalek AS, Alburyhi MM, Elaasser MM, Raslan AE. Metabolite Profiling and Toxicity, Antioxidant, and Antitumor Evaluation of Micromeria Biflora Aerial Parts Extract Combined with ADMET Prediction and Molecular Docking Analysis. Chemistry & Biodiversity., 2025; 0:e202403258:1-19.
31. 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.
32. 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.
33. Mohamed YAS, Hamidaddin MA, Yahya TA, Alkhawlani MA, Alburyhi MM. Phytochemical and Physicochemical Analysis of Yemeni Kalanchoe Marmorata Baker. World Journal of Pharmacy and Pharmaceutical Sciences., 2025; 14(9): 1024-1033.
34. 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.
35. Almamari A, Alburyhi MM, Alhag S. Species-Species Prevalence of Vaginal Candidiasis with Type 1 and Type 2 Diabetes Mellitus Among Women in Sana'a City. Journal of Chemical and Pharmaceutical Research., 2013; 5(8): 217-224.

36. 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.
37. Al-Ghani AM, Alkhawlani 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.
38. 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.
39. In-vitro evaluation of captopril tablets present in Yemen markets. Noman MA, Alburyhi MM, Saif AA, Omer KH. Research Journal of Pharmaceutical Dosage Forms and Technology., 2012; 4(2): 124-127.
40. 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.
41. Mohamed YAS, Alkhawlani MA, Faisal A, Alburyhi MM. Modern Analytical Techniques Used in Authentication of Yemeni Sider Honey. World Journal of Pharmacy and Pharmaceutical Sciences., 2025; 14(6): 1414-1429.
42. Mohamed YAS, Alkhawlani 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.
43. 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.
44. Alburyhi MM, Moharram BA. Formulation and Evaluation of Aloe Niebuhriana Extract as Naturaceutical Effervescent Granules Novel Drug Delivery Systems for Antidiabetic Activity. World Journal of Pharmaceutical Research., 2025; 14(18): 1147-1157.
45. 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.

46. 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.
47. 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.
48. Alburyhi MM, Raweh SM, AlGhoury ABA, Alkhawlani 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.
49. 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.
50. 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.
51. 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.
52. 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.
53. 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.
54. 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.

55. 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.
56. Abha, Kaur LP. Superdisintegrations: an Arising Exemplar in Orodispersible Tablets. Int J Drug Res Technol., 2015;5(1):1-12.
57. 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.
58. Stuart BH. Infrared Spectroscopy: Fundamentals and Applications. 1st ed. Wiley., 2004; p. S168.
59. 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.
60. 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.
61. 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.
62. Chadha R, Bhandari S. Drug–Excipient Compatibility Screening—Role of Thermoanalytical and Spectroscopic Techniques. J Pharm Biomed Anal., 2014; 87: 82-97.
63. O'Neill MA, Gaisford S. Application and Use of Isothermal Calorimetry in Pharmaceutical Development. Int J Pharm., 2011; 417: 83-93.
64. 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.
65. 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.
66. 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.
67. 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.

68. 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.
69. 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.
70. 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.
71. 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.
72. 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.
73. 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.
74. 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.
75. 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.
76. 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.
77. Raymond C. R, Sheskey PJ, Owen CS. Handbook of Pharmaceutical Excipients Fifth Edition Edited.
78. Shivangi S, Navneet V. Taste Masked Orodispersible Tablets. A highly patient Compliant Dosage Form. Asian J Pharm Clin Res., 2016; 9: 385-91.
79. Anupam R. Orodispersible Tablets: A Review. Asian J Pharm Clin Res., 2016; 9:19-26.

80. Abdelbary G, Eouani C, Prinderre P, Joachim J, Reynier J, Piccerelle P. Determination of The Invitro Disintegration Profile of Rapidly Disintegrating Tablets and Correlation with Oral Disintegration. Int J Pharm., 2005; 292: 29–41.
81. Anusha P, Nirajana A, Mohammed S, Jilani S, Murali C, Harish G. Development and Evaluation of Drotaverine Taste Masked Tablets with Improved Dissolution Efficiency Using Soild Dispersion Technique. IJRPB., 2013; 1: 275–80.
82. Srikanth M, Uhumwangho M, Sunil S, Sreenivasa N, Ravi C, Ramana Murthy K. Design and Revaluation of Taste Masked Drotaverine HCl Orodispersible Tablets Using Polymethacrylate Polymers. Der Pharmacia Lett., 2010; 2: 223–31.
83. Narasimhulu et al. Formulation and Evaluation of Orodispersible Drotaverine Sublingual Tablets. Indo American Journal of Pharm Sciences., 2014; 1(06).
84. Rele RV, Ruparel DG. UV Spent to Photo Metric Estimation of Drotaverine Hydrochloride by Derivative Method in Pharmaceutical Dosage Form. International Journal of ChemTech Research., 2018; aa (10): 353-360.
85. Shirwaikar AC. Galan Fast Disintegrating Tablets of Famotidine by Dry Granulation Method. Ind J Pharm Sci., 2004; 66: 422-426.
86. Venkateswarlu B, et al. Formulation and Evaluation of Famotidine Fast Dissolving Tablets by Direct Compression Method. Indian Journal of Research in Pharmacy and Biotechnology., 2013; 9-10(609): 609-613.
87. Sunada H, Bi YX. Preparation, Evaluation and Optimization of Rapidly Disintegrating Tablets. Powder Technol., 2002; 188–198.
88. https://go.drugbank.com/drugs/DB00787.
89. https:// pubchem.ncbi.nlm.nih.gov/compound/Acyclovir.
90. Reddy RA, Ramesh B. Kishan V. Drug-Excipient Interaction During Formulation Development In -Vitro and In -Vivo Evaluation of Gastroretentive Drug Delivery System for Nizatidine. Int J Pharm Sci Nanotech., 2013; 6: 2281-2293.
91. Prathyusha CH, Murthy TEGK. Compatibility Studies of Donepezil with Different Excipients by Using HPLC and FTIR. J Adv Pharm Tech Res., 2013; 3:273-278.
92. 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.
93. Shirwaikar AC. Galan Fast Disintegrating Tablets of Famotidine by Dry Granulation Method. Ind J Pharm Sci., 2004; 66: 422-426.

94. Chauhan I, Yasir M, Verma M, Singh AP. Nanostructured Lipid Carriers: A Groundbreaking Approach for Transdermal Drug Delivery. Advanced Pharmaceutical Bulletin., 2020; 10(2): 150.
95. Jones TM. Preformulation Studies., 2018.
96. Pereira MN, Schulte HL, Duarte N, Lima EM, Sá-Barreto LL, Gratieri T, Cunha-Filho MS. Solid effervescent formulations as new approach for topical minoxidil delivery. European Journal of Pharmaceutical Sciences., 2017; 96: 411-419.
97. Bary AA, El-Gazayerly ON, Alburyhi MM. A Pharmaceutical Study on Lamotrigine. Ph.D. Thesis, Faculty of Pharmacy, Cairo University., 2009.
98. 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.
99. 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.
100. 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.
101. 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.
102. 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.
103. 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.
104. 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.
105. 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.

106. 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.
107. 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.
108. 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.
109. 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.
110. 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.
111. 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.
112. 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.
113. 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.
114. 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.

115. 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.
116. 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.
117. 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.
118. 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.
119. Alburyhi MM, El-Shaibany A. Recent Innovations of Novel Drug Delivery Systems for Formulation, Development and Evaluation of Aloe Rubroviolaceae Extract Capsules as Naturaceutical for Hepatoprotective. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(4): 53-61.
120. 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.
121. 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.
122. 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.
123. 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.
124. 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.
125. 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.

126. 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.
127. 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.
128. 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.
129. 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.
130. 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.
131. 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.
132. 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.
133. Alburyhi MM, Saif AA, Noman MA. Formulation and Evaluation of Ticagrelor Orodispersible Tablets. World Journal of Pharmaceutical Research., 2024; 13(5): 26-55.
134. 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.
135. 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.
136. 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.

137. 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.
138. 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.
139. 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.
140. 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.
141. Bary AA, El-Gazayerly ON, Alburyhi MM. A Pharmaceutical Study on Methocarbamol. MSc Thesis, Faculty of Pharmacy, Cairo University., 2006.
142. 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.
143. 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.
144. 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.
145. 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.
146. 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.
147. 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.
148. 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.

149. 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.
150. 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.
151. Saif AA, Alburyhi MM, Noman MA. Formulation and Evaluation of Ketoprofen Fast Dissolving Tablets. International Journal of Sciences., 2018; 7(09):27- 39.
152. 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.
153. 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.
154. 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.
155. 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.
156. 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.
157. 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.
158. 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.

159. 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.
160. 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.
161. 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.
162. 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.
163. 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.
164. 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.
165. 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.
166. 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.
167. 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.
168. 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.
169. 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.

170. 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.
171. 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.
172. 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.
173. 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.
174. 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.
175. 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.
176. 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.
177. 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.
178. 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.

179. 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.
180. Nova MV, Janas C, Schmidt M, Ulshoefer T, Gräfe S, Schiffmann S, Bruschi ML. Nanocarriers for photodynamic therapy—rational formulation design and medium-scale manufacture. International Journal of Pharmaceutics., 2015; 491(1-2): 250-260.
181. KM AS, Natarajan J, Thirumaleshwar S, Kumar H. A review of the preparation, characterization and application of nanostructured lipid carriers. International Journal of Research in Pharmaceutical Sciences., 2020; 11(1): 1130-1135.
182. Varan G, Benito JM, Mellet CO, Bilensoy E. Development of polycationic amphiphilic cyclodextrin nanoparticles for anticancer drug delivery. Beilstein journal of nanotechnology., 2017; 8(1): 1457- 1468.
183. Chauhan I, Yasir M, Verma M, Singh AP. Nanostructured Lipid Carriers: A Groundbreaking Approach for Transdermal Drug Delivery. Advanced Pharmaceutical Bulletin., 2020; 10(2): 150.
184. Narvekar M, Xue HY, Eoh JY, Wong HL. Nanocarrier for poorly water-soluble anticancer drugs—barriers of translation and solutions. AapsPharmscitech., 2014; 15(4): 822-833.
185. Ghate VM, Kodoth AK, Raja S, Vishalakshi B, Lewis SA. Development of MART for the rapid production of nanostructured lipid carriers loaded with all-trans retinoic acid for dermal delivery. AAPS PharmSciTech., 2019; 20(4): 162.
186. Vieira AC, Chaves LL, Pinheiro M, Ferreira D, Sarmento B, Reis S. Design and statistical modeling of mannose-decorated dapsone-containing nanoparticles as a strategy of targeting intestinal M-cells. International journal of nanomedicine., 2016; 11: 2601.