

## COMPATIBILITY STUDIES OF SULFADOXINE WITH PHARMACEUTICAL EXCIPIENTS FOR THE DEVELOPMENT OF SUPPOSITORIES NOVEL DRUG DELIVERY SYSTEMS

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### ABSTRACT

The main objective of the present study was to the preformulation studies were performed to know the development of formulation and evaluation of Sulfadoxine antimalarial drugs in formulated suppositories Drug Delivery Systems. Sulfadoxine is classified as a biopharmaceutics classification system (BCS) Class-I. Preformulation, formulation and evaluation of Sulfadoxine to avoid problems associated with conventional delivery system such as limited permeation, low dissolution and bioavailability and also to improve bioavailability and one of the most antimalarial agents. In the present study that the compatibility was assessed by, FTIR spectroscopy, and melting point apparatus, precompression parameters. Results showed that physical mixtures of antimalarial and various excipients as PEG4000 base, Cocoa butter and Witepsol H35 were evaluated for preformulation studies parameters. It was concluded that the drug Sulfadoxine was found to be compatible with various excipients which were selected for the formulation development of the Sulfadoxine antimalarial drug in formulated suppositories Drug Delivery Systems. Formulation scientist from his experience and knowledge have to significantly in the preformulation study stage and is an important factor in the ADDS (Advanced Drug Delivery Systems) product development process.

**KEYWORDS:** Sulfadoxine, Compatibility, Suppositories, Preformulation, Formulation, Antimalarial drug.

### INTRODUCTION

#### Sulfadoxine<sup>[1-18]</sup>

Malaria is an infectious disease caused in human by the *Plasmodium spp.*, which infects erythrocytes. There are over one hundred species of the genus *Plasmodium*; however, only five of these have been shown to infect humans, viz. *P. vivax*, *P. ovale*, *P. knowlesi*, *P. malariae*, and the most prevalent, *P. falciparum*.

Recently *P. knowlesi*, has been causing tertian malaria in Malaysia and areas of Southeast Asia. Another species, *P. falciparum*, affects more erythrocytes than the other species and is much more serious and fatal within a few hours of the first symptoms.

Malaria remains a global public health problem affecting nearly half of the world's population. In the year 2020, global estimates indicated 241 million malaria cases and 627000-malaria deaths. In Yemen, 99% recorded cases had malignant malaria and annual incidence was not less than one million cases.<sup>[3]</sup> Most people diagnosed in the U.S. obtained their infection outside of the country,

usually while living or traveling through an area where malaria is endemic.

Chloroquine has been the drug of choice for protecting malaria infections. However, because of resistance, it is now only suggested for use in areas where *P. vivax*, *P. oval*, and *P. malaria* are present. *P. falciparum* that caused malignant malaria is becoming increasingly resistant to anti-malarial medications. For travelers going to areas where *P. falciparum* is endemic like in Yemen, there are several options for malaria prevention, including mefloquine, atovaquone/proguanil (Malarone), and doxycycline.

The most effective treatment for *P. falciparum* infection is the use of artemisinins in combination with other antimalarials (known as artemisinin-combination therapy, or ACT), which decreases resistance to any single drug component. These additional antimalarials include: amodiaquine, lumefantrine, mefloquine or Sulfadoxine /Pyrimethamine.

For severe malaria that caused by *P.falciparum*, artesunate is superior to quinine in both children and adults. In many parts of the world, for instance, resistance to Chloroquine has rendered the drug ineffective.

The suppository may be ideally used in: Babies or old people who cannot swallow oral medication and drugs destroyed by portal circulation.

The quantity of fluid available for drug dissolution is very small (approximately 3 ml). The rectal fluid is neutral in pH (7-8) and has no buffer capacity and when systemic effects are desired, greater absorption may be expected from an empty rectum as the drug will be in good contact with the absorbing surface of the rectum. Thus, the dissolution of slightly soluble substances is the slowest step in the absorptive process.

### Preformulation Studies<sup>[19-180]</sup>

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 Sulfadoxine - 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 Suppositories Drug Delivery Systems.

### MATERIALS AND METHODS

Sulfadoxine (Shaphaco Pharmaceutical Company-Yemen) all as a gift from (Shaphaco Pharmaceutical Company-Yemen), Cocoa Butter (M.O.H Kuwait), Witepsol H35 (Sasol gulf), Liquid paraffin, PEG 4000 as a gift from (Pharmacare Pharmaceutical Industry Company-Yemen).

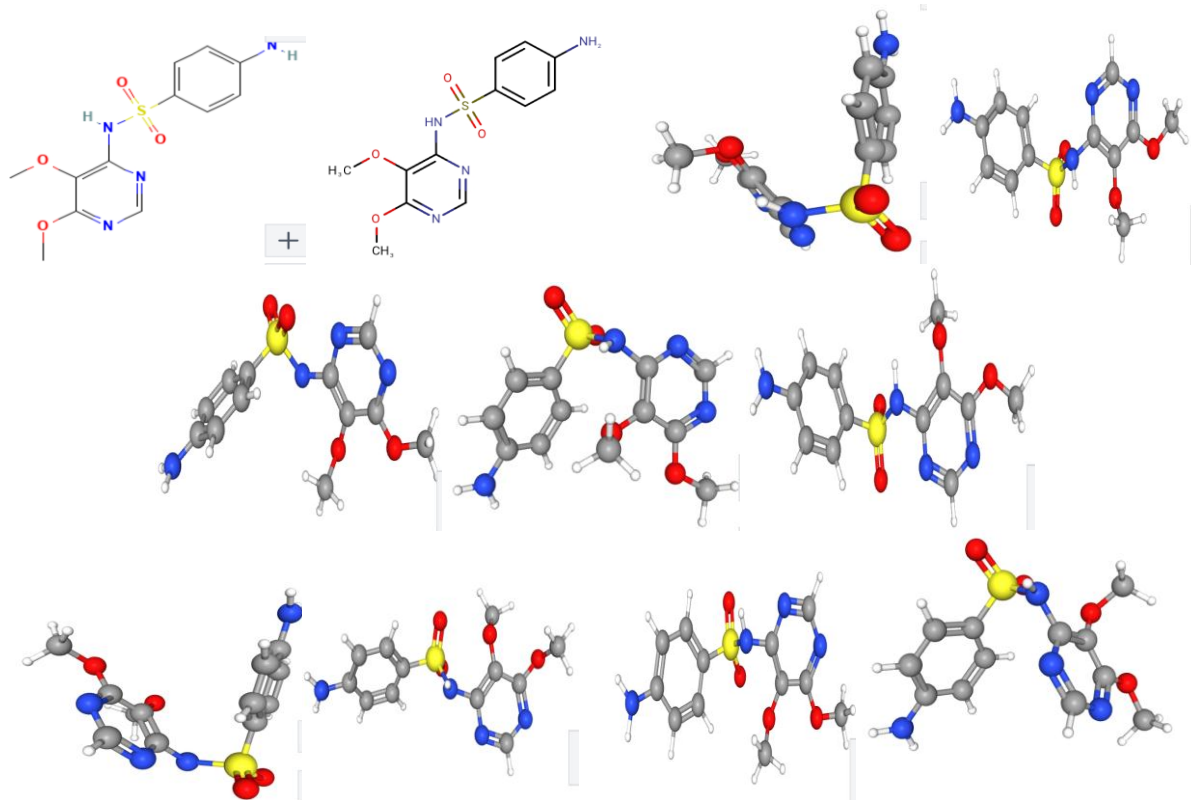
**Equipment's:** Melting point (Stuart scientific, U.K), I.R(FT/IR Spector, FT.IR), Heater (Assisistent, Schott, Germany), Balance (Germany).

## Preformulation Studies

Evaluation of Drug-Excipient Compatibility Studies Methods<sup>[35-240]</sup>

Table 1: Sulfadoxine Data.

## Characterization of Sulfadoxine



Sulfadoxine Structure and 3D Conformer

Chemical Structure	4-amino-N-(5,6-dimethoxypyrimidin-4-yl) benzenesulfonamide	Appearance	White or yellowish-white crystalline powder or crystals.
Molecular Formula	C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S	Drug Solubility	<b>Water Solubility:</b> very slightly soluble in water, slightly soluble in alcohol and in methanol. It dissolves in solutions of alkali hydroxides and in dilute mineral acids.
Molecular Weight	310.329 g/mol	BCS	Class-I.
Drug Action and Use	Antibacterial and Antimalaria: Is an ultra-long-lasting sulfonamide often used in combination with pyrimethamine to treat or prevent malaria. It is also used, usually in combination with other drugs, to treat or prevent various infections in livestock. Is a combination ant imalarial containing the sulfonamideanti bacterial Sulfadoxine and the antiparasitic pyrimethamine. Both drugs are anti folates; they inhibit the production of enzymes involved in the synthesis of folic acid within the parasites. Either drug by itself is only moderately effective in treating malaria, because the parasite Plasmodium falciparum may be able to use exogenous folic acid, i.e. folic acid which is present in the parasite's environment, while in combination, the two substances have a synergistic effect which outbalances that ability.		
Sulfadoxine Pharmacokinetics			
Drug Absorption	<b>Bioavailability:</b> Sulfadoxine oral tablets >90%.	Drug Distribution	<b>Volume Disrtbution:</b> 0.14L/kg. <b>Protien Binding:</b> about 90% protien bound.
Drug Metabolism	Sulfadoxine undergoes minimal metabolism by cytochrome P450 (CYP) enzymes.	Drug Excretion	Is excreted in the urine.
The Elimination Half-Life (T1/2)	The elimination half-life is about 100-230 hrs (7 to 9 days)	Availability	Tablets.



Table 2: Pharmaceutical Excipients Data.

Nonproprietary Name	Chemical Name	Functional Category	Concentration %	Solubility	Incompatibilities	Notes
Cocoa Butter	Theobrome	Suppository base		Insoluble in water	Cocoa butter can be incompatible with certain fats due to differences in triglyceride composition and polymorphic behavior.	<u>Polymorphism</u> , having $\alpha$ , $\gamma$ , $\beta'$ , and $\beta$ crystals
Polyethylene Glycol (PEG)	BP: Macrogols JP: Macrogol 400 Macrogol 1500 Macrogol 4000 Macrogol 6000 Macrogol 20000 PhEur: Macrogola USPNF: Polyethylene glycol	Ointment base; plasticizer; solvent; suppository base; tablet and capsule lubricant.		All grades of polyethylene glycol are soluble in water and miscible in all proportions with other polyethylene glycols (after melting, if necessary). Aqueous solutions of higher-molecular-weight grades may form gels. Liquid polyethylene glycols are soluble in acetone, alcohols, benzene, glycerin, and glycols. Solid polyethylene glycols are soluble in acetone, dichloromethane, ethanol (95%), and methanol; they are slightly soluble in aliphatic hydrocarbons and ether, but insoluble in fats, fixed oils, and mineral oil.	The chemical reactivity of polyethylene glycols is mainly confined to the two terminal hydroxyl groups, which can be either esterified or etherified. However, all grades can exhibit some oxidizing activity owing to the presence of peroxide impurities and secondary products formed by autoxidation. Liquid and solid polyethylene glycol grades may be incompatible with some coloring agents. The antibacterial activity of certain antibiotics is reduced in polyethylene glycol bases, particularly that of penicillin and bacitracin. The preservative efficacy of the parabens may also be impaired owing to binding with polyethylene glycols. Physical effects caused by polyethylene glycol bases include softening and liquefaction in mixtures with phenol, tannic acid, and salicylic acid. Discoloration of sulfonamides and dithranol can also occur and sorbitol may be precipitated from mixtures. Plastics, such as polyethylene, phenolformaldehyde, polyvinyl chloride, and cellulose-ester membranes (in filters) may be softened or dissolved by polyethylene glycols. Migration of polyethylene glycol can occur from tablet film coatings, leading to interaction with core components	The USPNF 23 describes polyethylene glycol as being an addition polymer of ethylene oxide and water. Polyethylene glycol grades 200–600 are liquids; grades 1000 and above are solids at ambient temperatures. Liquid grades (PEG 200–600) occur as clear, colorless or slightly yellow-colored, viscous liquids. They have a slight but characteristic odor and a bitter, slightly burning taste. PEG 600 can occur as a solid at ambient temperatures. Solid grades (PEG>1000) are white or off-white in color, and range in consistency from pastes to waxy flakes. They have a faint, sweet odor. Grades of PEG 6000 and above are available as free-flowing milled powders.

<b>Witepsol</b>	BP: Hard fat PhEur: Adeps solidus USPNF: Hard fat	Suppository base. The primary application of hard fat suppository bases, or semisynthetic glycerides, is as a vehicle for the rectal or vaginal administration of a variety of drugs, either to exert local effects or to achieve systemic absorption. Selection of a suppository base cannot usually be made in the absence of knowledge of the physicochemical properties and intrinsic thermodynamic activity of the drug substance. Other drug-related factors that can affect release and absorption and which must therefore be considered are the particle size distribution of insoluble solids, the oil : water partition coefficient, and the dissociation constant. The displacement value should also be known, as well as the ratio of drug to base. Properties of the suppository base that may or may not be modified by the drug, or that can influence drug release, are the melting characteristics, chemical reactivity, and rheology. The presence of additives in the base can also affect performance.	5–20% 20–90%	Freely soluble in carbon tetrachloride, chloroform, ether, toluene, and xylene; slightly soluble in warm ethanol; practically insoluble in water.	Incompatibilities with suppository bases are not now extensively reported in the literature. The occurrence of a chemical reaction between a hard fat suppository base and a drug is relatively rare, but any potential for such a reaction may be indicated by the magnitude of the hydroxyl value of the base.	A white or almost white, practically odorless, waxy, brittle mass. When heated to 508C it melts to give a colorless or slightly yellowish liquid.
<b>Liquid Paraffin</b>	BP: Liquid paraffin JP: Liquid paraffin	Heavy mineral oil; heavy liquid petrolatum; liquid	Ophthalmic ointments 3.0–60.0 %	Practically insoluble in ethanol (95%), glycerin,	Incompatible with strong oxidizing agents.	Mineral oil is a transparent, colorless,

	<p>PhEur: Paraffinum liquidum USP: Mineral oil.</p>	<p>petrolatum; paraffin oil; Sirius; white mineral oil. Emollient; lubricant; oleaginous vehicle; solvent. Mineral oil is used primarily as an excipient in topical pharmaceutical formulations, where its emollient properties are exploited as an ingredient in ointment bases. It is additionally used in oil-in-water emulsions, as a solvent, and as a lubricant in capsule and tablet formulations, and to a limited extent as a mold-release agent for cocoa butter suppositories. It has also been used in the preparation of microspheres. Therapeutically, mineral oil has been used as a laxative. Mineral oil is used in ophthalmic formulations for its lubricant properties. It is also used in cosmetics and some food products.</p>	<p>Otic preparations 0.5–3.0% Topical emulsions 1.0–32.0% Topical lotions 1.0–20.0% Topical ointments 0.1–95.0%.</p>	<p>and water; soluble in acetone, benzene, chloroform, carbon disulfide, ether, and petroleum ether. Miscible with volatile oils and fixed oils, with the exception of castor oil.</p>		<p>viscous oily liquid, without fluorescence in daylight. It is practically tasteless and odorless when cold, and has a faint odor of petroleum when heated.</p>
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According to Sulfadoxine and excipients data as shown in Tables 1 and 2, it was selected that the different excipients to preformulation study with Sulfadoxine in the present study.

### Suppository Formulations

As shown in Tables 3 and 4.

**Table 3: Preparation of Suppository Formulations of Sulfadoxine.**

Bases	Sulfadoxine
(F1) Cocoa B	Rx Sulfadoxine 8gm Cocoa butter 7.895gm
(F2) Witepsol H35	Rx Sulfadoxine 8gm Witepsol 8.2gm
(F3) PEG4000	Rx Sulfadoxine 8gm PEG 7.6gm
(F4) Cocoa Butter & Witepsol H35	Rx Sulfadoxine 8gm Cocoa butter 4.01gm Witepsol 4.01gm
(F5) Cocoa Butter & PEG4000	Rx Sulfadoxine 8gm Cocoa butter 4.05 gm PEG 4.05gm
(F6) Witepsol H35 & PEG4000	Rx Sulfadoxine 8gm Witepsol 3.8gm PEG 3.8gm

**Table 4: Calculate of Chloroquine Phosphate Formulations.**

Name of Base	Cocoa Butter	Witepsol	PEG 4000C	Cocoa Butter+ Witepsol	Cocoa Butter+ PEG	PEG+ Witepsol
Wt.of drug = con.xno.of supp.Xcapacity ofmould	0.5x8x2=8	0.5x8x2=8	0.5x8x2=8	0.5x8x2=8	0.5x8x2=8	0.5x8x2=8
Amount of base = wt. of drug/D.V	8/0.987= 8.1053	8/1.0256= 7.80031	8/0.952= 8.4	8/1.0025= 7.98	8/1.012= 7.9	8/0.952= 8.4
Amount of base for drug	8-8.1053= 0.1053	8-7.80031= 0.2	8-8.4= 0.4	8-7.98= 0.02	8-7.9= 0.1	8-8.4= 0.4
Theoretical correction of D.V	8+0.1053= 8.1	8+0.2= 8.2	8+0.4= 8.4	8+0.02= 8.02	8+0.1= 8.1	8+0.4= 8.4

\*Each Suppositories Contain 1000mg of Sulfadoxine.

### Preformulation Studies

Preformulation studies are initiated to define the physical and chemical properties of the agent. The key goals of preformulation studies are to ensure the delivery of drug product with acceptable stability, bioavailability, and manufacturability.

### Melting Point Determination of Sulfadoxine

The most common and most basic method of determination is the capillary method. Melting point of the Sulfadoxine 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.

### Drug-Excipient Compatibility Studies

A physical mixture including Sulfadoxine and excipient was created in a 1:1 ratio, and it was subjected to analytical techniques such as FTIR spectroscopy. FTIR, of both pure drug and physical mixes were obtained, and the spectra of the both drug and mixture of excipient with drug were compared to look for any incompatibilities.

### FTIR Spectroscopy Study

FTIR study KBr-disc method was used to record the FTIR spectra and KBr pellets were made in 1:100 ratio of sample and KBr. FTIR spectra was recorded using FTIR spectrum in a range of 4000-400cm<sup>-1</sup>. Different functional groups of test compound for distinctive vibrational frequencies are identified using FTIR spectroscopy. FTIR spectra were used for the



investigation of interaction in the physical mixture of API and excipient through shifting of peaks to lower or higher wavenumbers and appearance or disappearance of characteristic peaks of functional groups for pure API in physical mixture. FTIR spectroscopic study was performed to check the compatibility between API, and different excipients in ratio (1:1). The FTIR spectra of a API alone and API with excipients were obtained by KBr method and compared with the standard FTIR spectrum of the pure API. Infrared spectrophotometer is not only used for determining the compatibility of excipients with the APIs, but also for API identification.

#### Preparation of IR Samples

The sample was determined by the disc method. Triturate 5mg of the substance to be examined with 300-400 mg of finely powdered and dried potassium bromide R or potassium chloride R. Each excipient was mix with Sulfadoxine equally then of potassium bromide is added to the mixture. Carefully grind the mixture, spread it

uniformly in a suitable die, and submit it to a pressure of about 800 MPa ( $8 \text{ t}\cdot\text{cm}^{-2}$ ). Then the tablets were inserted to the device and the Infrared spectra was recorded at mild-infrared light in wavenumber range of  $4000 \text{ cm}^{-1}$  to  $400 \text{ cm}^{-1}$ . After that the spectra were compared with the reference.

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

Compatibility studies were performed by preparing blend of different excipients with Sulfadoxine in room condition.

## RESULTS AND DISCUSSION

### Preformulation Studies

#### Characterization of Sulfadoxine

The organoleptic properties of Sulfadoxine were shown in Table 5.

**Table 5: Physicochemical Parameters of The Suppositories of Sulfadoxine Formulations.**

Drug	Type of Base	Shape	Color	Consistency	Disintegration Time	Average Weight
Sulfadoxine	F1	Bullet Shape	Pale Yellow	Hard Melt	5min	Within Limit
	F2	Bullet Shape	White	Hard	6 min	Within Limit
	F3	Bullet Shape	White	Hard	45 min	Within Limit
	F4	Bullet Shape	White Above and Yellow Bottom	Hard	45min	Within Limit
	F5	Bullet Shape	White Above and Yellow Bottom	Hard	5min	Within Limit
	F6	Bullet Shape	White	Hard	6min	Within Limit

#### Melting Point Determination of Sulfadoxine

Melting point of pure Sulfadoxine was determined by open capillary method. The capillary tube was closed at one end by fusion and was filled with Sulfadoxine 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 Sulfadoxine was identical to reference melting point stated in MP (98-100°C). The sample started to melt at 98°C, and turned into liquid at 99°C, indicating that the sample used is pure. That reading has stated in melting point tester.as shown in Table 6.

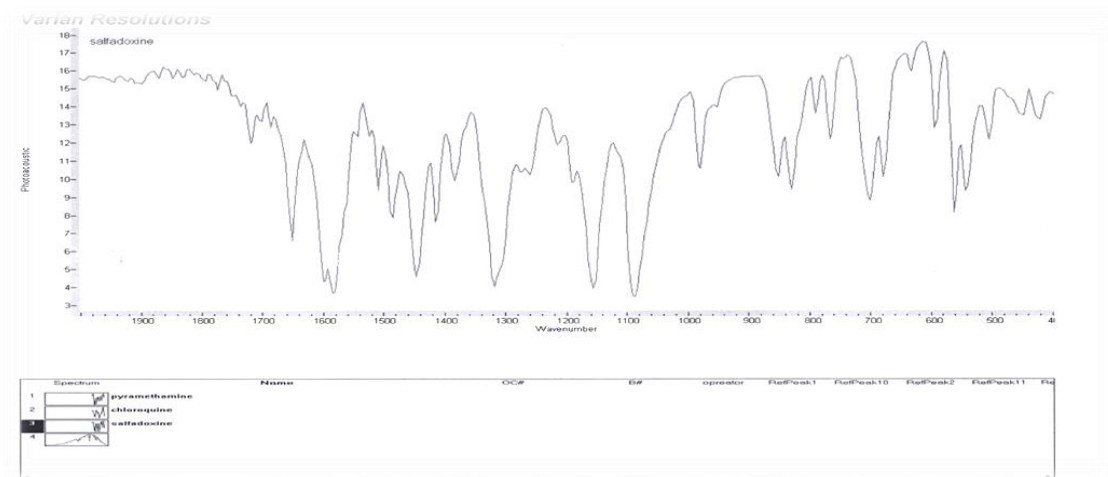
**Table 6: Results of Melting Point of Sulfadoxine.**

Test	Temp Rang Analyzed (Melting )	Results
Test I Sulfadoxine	(98-100°C)	99°C
Test II Sulfadoxine	(98-100°C)	99°C

#### Characterization of Sulfadoxine by FTIR

FTIR spectrum studies indicated that major functional groups present in Sulfadoxine show characteristic peaks in IR spectrum. Figure (1) show peaks observed at different wave numbers and the functional group

associated with these peaks for drug. The major peaks are identical to functional group of Sulfadoxine. Hence, it was confirmed that there was compatibility between drug and various excipients.



**Fig. 1: FTIR Spectrum of Pure Sulfadoxine.**

## CONCLUSION

The compatibility studies of physical mixtures of Sulfadoxine with different used excipients such as PEG4000 base, Cocoa butter and Witepsol H35 were investigated by FTIR it was detected that there was no variation or minor deviation in the characteristic peaks in FTIR spectroscopy. The Sulfadoxine formulations prepared were evaluated for precompression parameters and powder flow properties which were found to be within limits. It was concluded that the drug Sulfadoxine was found to be compatible with various excipients which were selected for the formulation development of the Sulfadoxine antimalarial drugs in formulated suppositories Drug Delivery Systems. Formulation scientist from his experience and knowledge have to significantly in the preformulation study stage and is an important factor in the ADDS (Advanced Drug Delivery Systems) product development process.

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