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Systematic Preformulation Studies and Drug-Excipient Compatibility Evaluation of Abacavir Sulphate for Design of Gastroretentive Floating Drug Delivery System.

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ABSTRACT

Background: Gastroretentive floating microspheres offer promising approach for sustained delivery of antiretroviral drugs. Comprehensive preformulation studies are essential for rational formulation development and selection of compatible excipients.

Objective: To conduct systematic preformulation studies of Abacavir sulphate for development of gastroretentive floating microspheres and evaluate drug-excipient compatibility with selected polymers.

Methods: Preformulation studies including organoleptic properties, flow properties (angle of repose, bulk density, tapped density, compressibility index, Hausner ratio), melting point, pH, and solubility were performed as per standard procedures. Drug-excipient compatibility was evaluated by physical observation under accelerated stability conditions (40°C/75%RH and 60°C) and FTIR spectroscopy using HPMC K4M and HPMC K100M polymers.

Results: Abacavir sulphate appeared as off-white odorless powder with melting point 165°C. The drug exhibited poor flow properties with angle of repose 29°28", compressibility index 28.04%, and Hausner ratio 1.34. The aqueous solution showed neutral pH (7.5) and drug was freely soluble in water. Compatibility studies revealed no physical changes after one month storage at accelerated conditions. FTIR analysis showed characteristic peaks at 3463.2, 2958.6, 2849.7, 1660.0, and 1451.6 cm^{-1}. No interaction was observed between drug and polymers as all characteristic peaks were retained in mixture spectrum.

Conclusion: Preformulation studies confirmed suitability of Abacavir sulphate for gastroretentive microsphere development. The drug showed good compatibility with HPMC K4M and K100M polymers, supporting their use in formulation design.

Keywords: *Abacavir sulphate, preformulation, gastroretentive microspheres, HPMC, drug-excipient compatibility, FTIR*

INTRODUCTION

Abacavir sulfate is a water-soluble nucleoside reverse transcriptase inhibitor, a promising candidate for gastro-retentive floating delivery due toits relatively short plasma half-life and better absorption in the upper gastrointestinal tract[1]. However, formulation of abacavir sulfate floating microspheres poses several interdependent physical and chemical pre-formulation challenges. These challenges are required to be addressed during pre-formulation stage to avoid formulation failure, ensuring reproducible in-vitro and in-vivo performance of resulting formulation[2].

The primary challenges are related to its physical properties, majorly density control.The floating microspheres must have sufficiently low bulk and true density as well as controlled porosity to remain buoyant in gastric fluid for extended periods[3]. Achieving that while maintaining acceptable drug loading is nontrivial drugs are challenging due to higher drug loading which tends to raise particle density. This can produce non-buoyant fractions or variable floating lag times. Particle size and size distribution are also critical[4]. Extensively small particles may be rapidly emptied, too large and they can have poor dose uniformity and altered release kinetics. Related powder physical properties like flowability, compressibility, and tendency to agglomerate must be characterized since microspheres with poor flow results in dose variability and scale-up

issues[1]. Process variables in common preparation methods (emulsion-solvent diffusion/evaporation, spray-drying, or non-aqueous solvent evaporation) strongly influence granules morphology, hollow core formation, and porosity[5]. Thus, pre-formulation study should target solvent choice, evaporation rate, stirring shear, and polymer solution viscosity as critical CPPs (critical process parameters)[5]

Abacavir sulfate demonstrated susceptibility to degradation under certain stress conditions in terms of hydrolysis and oxidative pathways have been reported[6]. Drug-polymer/excipient compatibility studies are also required for successful formation.Some commonly used matrix polymers (e.g., HPMC, ethyl cellulose, Eudragit grades) and plasticizers may show physical or chemical incompatibility with the API, alter release rate or promoting degradation products[5]. Photostability and oxidative stability should be assessed because radical-forming excipients or trace metals in polymers can catalyze degradation during storage[7].

Preformulation studies should thus be systematic. Characteristics of the solid-state should be thoroughly evaluated (XRPD to look for polymorphism or amorphous content, DSC to understand melting and glass transitions, and FTIR to probe any functional groups that might be susceptible)[2]. Measure parameters such as pKa, intrinsic solubility (as a function of pH - namely gastric pH 1–3 and intestinal pH 6–7.5), log P, and the partitioning behavior of the drug into polymeric matrices. Conduct forced-degradation studies (acid-base, oxidative, thermal, photolytic, and stressing in the relevant solvents) to identify susceptible moieties and to select antioxidants, chelators, or pH-modifiers. Because moisture uptake can cause collapse of hollow microspheres or accelerate hydrolysis, measures of hygroscopicity and moisture sorption isotherms will be useful.

Compatibility studies (binary mixtures with proposed polymers, surfactants, and common capsule/tablet excipients) using DSC/FTIR and short-term stressed mixtures help in selection of compatible excipients[5]. For buoyancy engineering, preformulation studies should evaluate polymer combinations that offer low density (e.g., ethyl cellulose, HPMC combinations, or gas-generating excipient systems) while enabling controlled drug release. The effect of polymer:drug ratio on encapsulation efficiency, porosity and in-vitro floating lag and duration are also crucial.

Finally, it is a good idea to develop the relevant analytical tools early: a stability-indicating HPLC/UHPLC procedure for abacavir and the known degradation products is a must (quantitation and forced degradation studies) and some buoyancy and in vitro release studies (depending on lot size; i.e., simulated gastric fluid with proper agitation) to correlate formulation variables to floating and release[8]. Together, the collected information from the preformulation studies will allow for reasoned decision making in the selection of the encapsulation method, polymer system, stabilizing excipients (antioxidant, desiccant), and packaging in order to generate floatable, stable, and scalable abacavir microspheres.

MATERIALS AND METHODS

Abacavir sulphate was obtained from Apotex Laboratories. Bangalore, India as a gift sample.HPMC K4M and HPMC K100M were obtained from pharmaceutics research lab of university. Methanol, dichloromethane, ethanol, DMSO, and Tween 80 were obtained from analytical research laboratory. All other chemicals and reagents used were of analytical grade.The organoleptic properties of Abacavir sulphate were evaluated by visual inspection. The drug sample was observed for its color, odor, and appearance. The results were recorded and compared with standard specifications.

Angle of Repose

The angle of repose was determined by fixed funnel method. The drug powder was allowed to flow through a funnel fixed at a specific height. The powder formed a cone shape on the flat surface. The height (h) and radius (r) of the powder cone were measured. The angle of repose (θ) was calculated using the following formula [9]:

$\theta = \tan^{-1} (h/r)$

Where,

h = height of the pile

r = radius of the pile

The flow properties were interpreted according to standard scale. An angle of repose less than 30° indicates excellent flow, 30-35° shows good flow, 35-40° indicates fair flow, and more than 40° shows poor flow properties[10].

Bulk Density

Bulk density was determined by pouring the drug powder into a graduated measuring cylinder. A known quantity of powder (approximately 10 gm) was carefully transferred into the cylinder. The volume occupied by the powder was noted without any tapping. The bulk density was calculated using the formula [11]:

Bulk Density = Mass of powder / Bulk volume

The result was expressed in gm/ml.

Tapped Density

For tapped density determination, the same graduated cylinder containing the powder was tapped mechanically for about 500 times or until no further change in volume was observed. The final volume was recorded as tapped volume. The tapped density was calculated using the formula [12]:

Tapped Density = Mass of powder / Tapped volume

The result was expressed in gm/ml.

Compressibility Index (Carr's Index)

The compressibility index is a measure of the powder's ability to settle, and it permits an assessment of the relative importance of interparticulate interactions. The compressibility index was calculated using the formula [7]:

Compressibility Index (%) = [(Tapped Density - Bulk Density) / Tapped Density] × 100

The flow property was assessed based on the compressibility index values. Values less than 10% indicate excellent flow, 11-15% show good flow, 16-20% indicate fair flow, 21-25% show passable flow, 26-31% indicate poor flow, 32-37% show very poor flow, and more than 38% indicates very very poor flow[13].

Hausner Ratio

Hausner ratio is an indirect index of ease of powder flow. It was calculated by the following formula [14]:

Hausner Ratio = Tapped Density / Bulk Density

A Hausner ratio less than 1.25 indicates good flow properties, while greater than 1.25 shows poor flow properties. The value between 1.25-1.5 indicates moderate flow [14], [15].

Melting Point Determination

The melting point of Abacavir sulphate was determined by capillary tube method using melting point apparatus. A small amount of drug powder was filled in a capillary tube sealed at one end. The capillary tube was placed in the melting point apparatus and heated gradually. The temperature at which the drug started melting and completely melted was noted as melting point range[16].

pH Determination

The pH of drug solution was determined using digital pH meter. A 1% w/v solution of Abacavir sulphate was prepared in distilled water. The pH meter was calibrated using standard buffer solutions of pH 4.0 and 7.0 before measurement. The electrode was dipped in the drug solution and pH value was recorded[11].

Solubility Studies

The solubility of Abacavir sulphate was determined in various solvents including water, methanol, ethanol, and DMSO. Excess amount of drug was added to 10 ml of each solvent in separate glass vials. The vials were kept at room temperature for 24 hours with occasional shaking. The solutions were then filtered and observed for solubility. The solubility was classified according to IP standards as freely soluble, soluble, sparingly soluble, slightly soluble, very slightly soluble, and practically insoluble [16].

Drug-Excipient Compatibility Studies

Physical Compatibility Studies

The physical compatibility between drug and excipients was studied by storing the mixtures under accelerated stability conditions. The drug was mixed with individual excipients in 1:1 ratio and filled with glass vials. The vials were stored in different conditions:

40°C ± 2°C / 75% ± 5% RH

60°C ± 2°C

The samples were observed initially and after 1 month for any physical changes like color change, liquefaction, or caking [17].

FTIR Spectroscopy

Fourier Transform Infrared (FTIR) spectroscopy was performed to study chemical interaction between drug and polymers. FTIR spectra were recorded for pure drug, individual polymers (HPMC K4M and HPMC K100M), and physical mixture of

drug with polymers. The samples were prepared by KBr pellet method. The pellets were scanned in the range of 4000-400 cm^{-1} using FTIR spectrophotometer. The characteristic peaks were noted and compared to identify any interaction [18].

RESULTS

The preformulation studies were performed to design the formulation of abacavir. The solubility of AS was performed in various solvents likewater, methanol, ethanol, and DMSOas mentioned in table 1.The standard cure was prepared 0.1 N HCl at 296 nm as shown in figure 1.

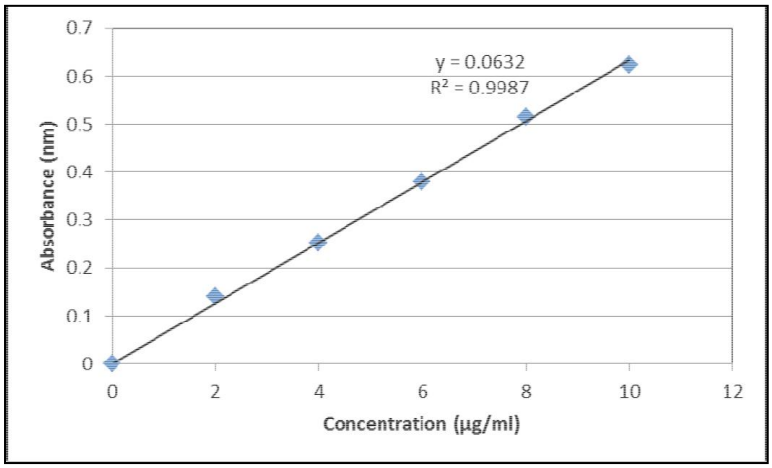

Figure 1. Standard curve for Abacavir sulphate in 0.1 N HCl.

Organoleptic Properties

The organoleptic evaluation of Abacavir sulphate is presented in Table 1. The drug appeared as off-white colored powder with no characteristic odor. These observations were found to be within the specified limits and comply with the standard specifications.

Table 1: Organoleptic Properties of Abacavir Sulphate

Test	Specifications/Limits	Observations
Color	White to off white	Off White powder
Odour	Odorless	Odorless

The results complywith specifications**.**

Flow Properties

Angle of Repose

The angle of repose for Abacavir sulphate was found to be 29°28" as shown in Table 15. According to the standard classification, an angle of repose in the range of 25-30° indicates good flow properties, however values approaching 30° suggest borderline poor flow characteristics [9]. The angle of repose was found to be 29°28".The result shows that drug having poor flow properties**.**

Bulk Density and Tapped Density

The bulk density and tapped density values of Abacavir sulphate are presented in Table 2. The bulk density was found to be 0.19 gm/ml and tapped density was 0.26 gm/ml. The difference between these two values indicates the packing characteristics of the powder.

Table 2: Density Values of Abacavir Sulphate

Materials	Bulk Density (gm/ml)	Tapped Density (gm/ml)
Abacavir sulphate	0.19	0.26

Powder Compressibility

The compressibility index and Hausner ratio of Abacavir sulphate are shown in Table 3. The compressibility index was calculated as 28.04% and Hausner ratio was 1.34. According to USP classification, compressibility index between 26-31% indicates poor flow and Hausner ratio greater than 1.25 also confirms poor flow properties[12].

Table 3: Powder Compressibility Parameters

Material	Compressibility Index	Hausner Ratio
Abacavir sulphate	28.04%	1.34

The results shows that drug having poor flow property.

Melting Point

The melting point of Abacavir sulphate was determined and results are presented in Table 4. The drug showed melting point at 165°C which complies with the reported literature value. Sharp melting point indicates the purity of drug sample [16].

Table 4: Melting Point of Abacavir Sulphate

Material	Melting Point Range	Result
Abacavir sulphate	165°C	Complies

The result complies as per specification**.**

Solution Properties

pH of Solution

The pH of 1% w/v aqueous solution of Abacavir sulphate was found to be 7.5 as shown in Table 5. This indicates that the drug solution is neutral in nature, which is important for gastric tolerance and stability considerations[19].

Table 5: pH of Abacavir Sulphate Solution

Material	Test	Specification	Observation
Abacavir sulphate	pH	7.5	7.5

The result complies as per specification.

Solubility Studies

The solubility behavior of Abacavir sulphate in different solvents is presented in Table 6. The drug was found to be freely soluble in water, which is advantageous for formulation development. It showed sparingly soluble nature in DMSO, ethanol, and methanol.

Table 6: Solubility Profile of Abacavir Sulphate

Test	Specification	Result
Solubility	Freely soluble in water, sparingly soluble in DMSO, ethanol, methanol	Complies

The result complies as per specification.

Drug-Excipient Compatibility Studies

Physical Compatibility

Drug excipient interactions play a vital role with respect to release of drug from formulation amongst others. FTIR techniques have been used here to study the physical and chemical interaction between drug and excipient used.

The results of physical compatibility studies are presented in Table 7. All the drug-excipient mixtures were stored at 40°C/75%RH and 60°C for one month. No physical changes such as color change, caking, or liquefaction were observed in any of the samples. This indicates good physical compatibility between drug and selected excipients[17].

Table 7: Drug-Excipients Compatibility Study Results

Drug + Excipients	Initial	After 1 month at40°C/75%RH	After 1 month at 60°C	Compatible
Drug	White powder	No change	No change	Yes
Drug + Methanol	White powder	No change	No change	Yes
Drug + Tween 80	White powder	No change	No change	Yes
Drug + HPMC K100M	White powder	No change	No change	Yes
Drug + HPMC K4M	White powder	No change	No change	Yes
Drug+ Dichloromethane	White powder	No change	No change	Yes

FTIR Spectroscopy Studies

FTIR spectroscopy was performed for pure Abacavir sulphate, individual polymers (HPMC K4M and HPMC K100M), and physical mixture of drug with polymers. The IR spectra are shown in Fig. 2(a), 2(b), 2(c), and 2(d).

The FTIR spectrum of pure Abacavir sulphate showed characteristic peaks at different wave numbers. The major peaks and their assignments are presented in Table 8.

Table 8: Band Assignments for the Infrared Absorption Spectrum of Abacavir Sulphate.

Band Energy (cm^{-1})	Assignment
3463.2	Tertiary amine hydrochloride (N-H) stretch
2958.6	O-H stretch
2849.7	C-H Stretch
1660.0	Cyclopentene Ring C=C stretch
1451.6	C-H Bending (CH_2 Scissoring)

The FTIR spectrum of pure drug showed characteristic absorption bands at 3463.2 cm^{-1} for N-H stretching of tertiary amine hydrochloride, 2958.6 cm^{-1} for O-H stretching, 2849.7 cm^{-1} for C-H stretching, 1660.0 cm^{-1} for C=C stretching of cyclopentene ring, and 1451.6 cm^{-1} for C-H bending vibrations[2].

The FTIR spectra of HPMC K4M and HPMC K100M showed their characteristic peaks. When the FTIR spectrum of physical mixture of drug with polymers was compared with pure drug spectrum, all the characteristic peaks of drug were present without any significant shift. No new peaks were observed in the mixture spectrum. This indicates absence of any chemical interaction between drug and polymers.

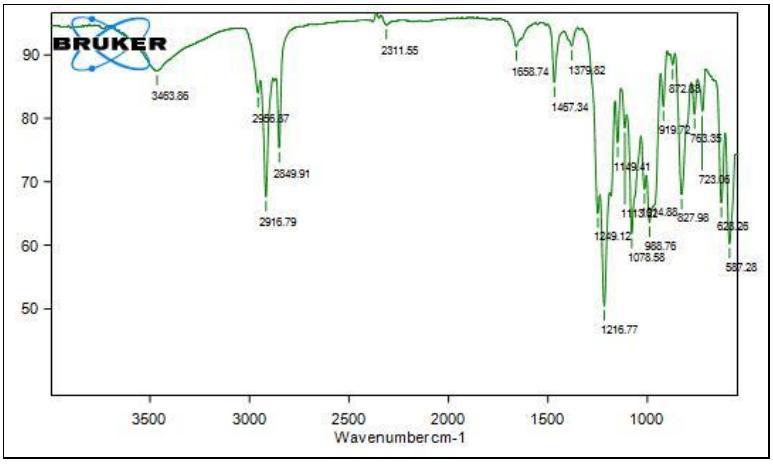

Figure 2(a) FT-IR of Abacavir Sulphate.

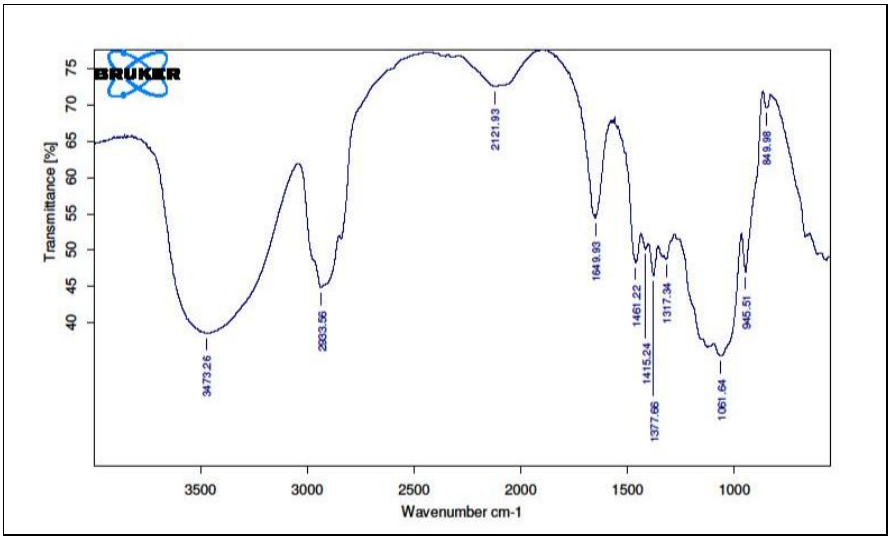

Figure 2(b) FT-IR Graph of HPMC K4M.

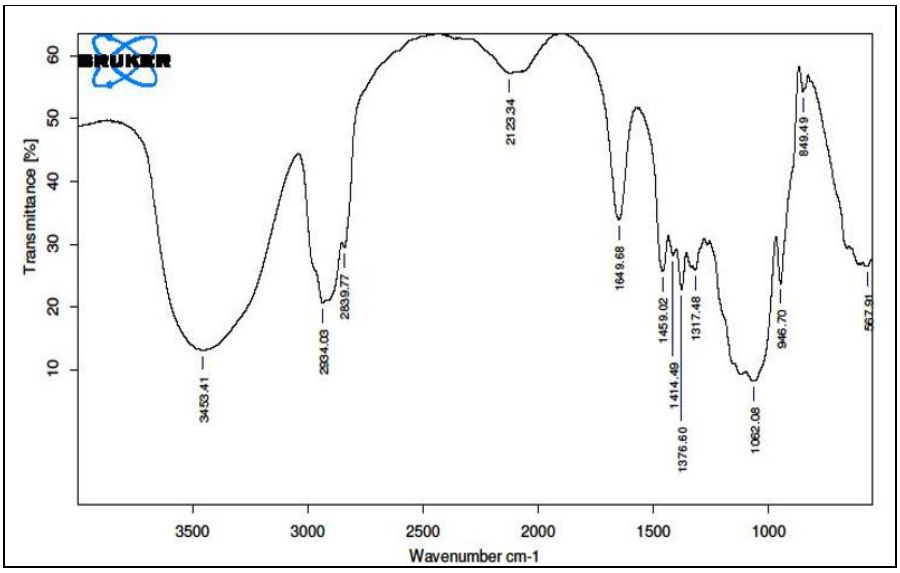

Figure 2(c) FT-IR Graph of HPMC K100M

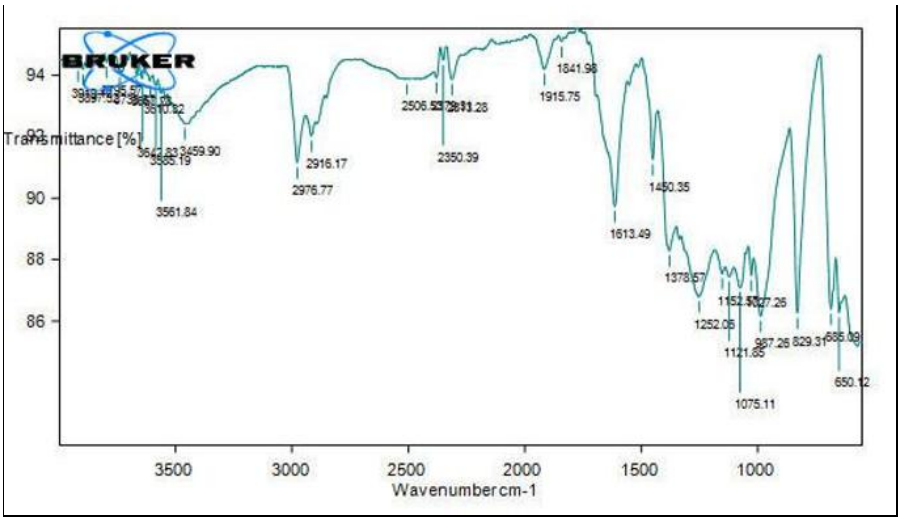

Figure 2(d) FT-IR Graph of Mixture ofAbacavir Sulphate + HPMC K4M +HPMC K100M.

In the present study, it has been observed that there is no chemical interaction between Abacavir sulphate and the polymers used. From the figures 2(a),2(b), 2(c) and 2(d) it was observed that there were no changes in these main peaks in IR spectra of mixture of drug and polymers, which show there were no physical interactions because of some bond formation between drug and polymer.

DISCUSSION

Preformulation studies involving organoleptic bulk density, tapped density, angle of repose, compressibility of index, Hausner ratio, melting point range, pH, solubility was carried out as per IP specification.Drug excipient compatibilities were carried out and evaluation and FT-IR, SEM. This showed no significant change in any way to the Mixture.

Different polymers like sodium alginate, sodium carboxy methyl cellulose, HPMC K4M, HPMC K100M were utilized in the trials. All the physical evaluations are carried in preformulation studies were carried out on all the three different polymers utilized. All the formulations exhibited values within the acceptable range.

Preformulation studies are important investigations carried out before formulation development to establish the physicochemical properties of drug substances. These studies help in selecting suitable excipients and developing stable formulations[1], [3]. In the present study, comprehensive preformulation studies were conducted for Abacavir sulphate to develop gastroretentive microspheres.

The organoleptic evaluation revealed that Abacavir sulphate is an off-white-colored powder without any characteristic odor. These observations matched the reported specifications. Organoleptic properties are important for identification of drug and quality control purposes[16].

The flow properties of powder are crucial for processing and manufacturing operations. Poor flow can lead to problems during powder transfer, mixing, and filling operations [11]. The angle of repose for Abacavir sulphate was found to be 29°28", which indicates borderline poor flow properties. Generally, powders with angle of repose below 30° are considered to have good flow, but values close to 30° suggest flow issues may occur [9].

The bulk density value of 0.19 gm/ml and tapped density of 0.26 gm/ml indicate the packing behavior of the powder. The significant difference between these values suggests that the powder undergoes considerable volume reduction upon tapping, which is characteristic of poor flowing materials [12].

The compressibility index of 28.04% falls in the range of 26-31%, which according to USP classification indicates poor flow properties. Similarly, the Hausner ratio of 1.34 (greater than 1.25) also confirms poor flow characteristics. These parameters suggest that the powder particles have high inter-particulate friction and cohesiveness [14], [15].

The poor flow properties of Abacavir sulphate can be attributed to its fine particle size and irregular shape. Such powders require the addition of glidants during formulation to improve flow properties. Commonly used glidants include colloidal silicon dioxide, talc, and magnesium stearate [7]. Similar observations were reported by Sharma et al., where they found that addition of 0.5% colloidal silicon dioxide significantly improved the flow properties of poorly flowing drugs[10].

The melting point of Abacavir sulphate was observed at 165°C, which matches with the reported literature values. A sharp melting point without decomposition indicates good purity of the drug sample. This parameter is important for thermal analysis and processing conditions selection. The drug remains stable at normal processing temperatures used in pharmaceutical manufacturing [16]. Drugs with melting point above 150°C are generally thermally stable during common pharmaceutical processing operations[13].

The pH of 1% w/v aqueous solution was found to be 7.5, indicating neutral nature of the drug solution. This is favorable for gastroretentive formulations as neutral pH minimizes gastric irritation and maintains stability in acidic environment of stomach. Many drugs undergo pH-dependent degradation, but neutral pH of Abacavir sulphate solution suggests good stability profile[19]. A recent study demonstrated that drugs with neutral pH show better gastric tolerance and reduced side effects in gastroretentive formulations[20].

The solubility studies revealed that Abacavir sulphate is freely soluble in water, which is highly advantageous for formulation development. High aqueous solubility ensures rapid dissolution and good bioavailability. The drug showed sparingly soluble nature in organic solvents like methanol, ethanol, and DMSO. This solubility profile is suitable for developing various dosage forms including immediate release and sustained release formulations[16]. Garg et al., reported that drugs with high aqueous solubility (>10 mg/ml) are ideal candidates for controlled release delivery systems[20].

Drug-excipient compatibility studies are essential to ensure the stability and efficacy of final formulation. Incompatibility between drug and excipients can lead to degradation of drug, loss of potency, and formation of toxic products [17]. According to Bharate et al.preformulation compatibility studies help in early detection of potential incompatibilities and save time and resources during formulation development[21].

The physical compatibility studies conducted under accelerated conditions (40°C/75%RH and 60°C) for one month showed

no visible changes in any of the drug-excipient mixtures. No color change, liquefaction, or caking was observed. This indicates good physical stability and compatibility between Abacavir sulphate and selected excipients including HPMC K4M, HPMC K100M, Tween 80, methanol, and dichloromethane. Similar methodology was employed by Garg et al., (2013) for compatibility screening of antiretroviral drugs with polymers[20].

FTIR spectroscopy is a powerful tool for detecting chemical interactions between drug and excipients. The technique identifies functional groups and chemical bonds based on their characteristic absorption frequencies[2]. In the present study, pure Abacavir sulphate showed characteristic peaks at 3463.2 cm^{-1} (N-H stretch), 2958.6 cm^{-1} (O-H stretch), 2849.7 cm^{-1} (C-H stretch), 1660.0 cm^{-1} (C=C stretch of cyclopentene ring), and 1451.6 cm^{-1} (C-H bending).

When the FTIR spectrum of physical mixture was compared with pure drug spectrum, all the major peaks of drug were retained without significant shift or disappearance. No new peaks appeared in the mixture spectrum. This confirms that there is no chemical interaction between Abacavir sulphate and the polymers used (HPMC K4M and HPMC K100M). The presence of all characteristic peaks in the mixture indicates that the drug maintains its chemical identity and stability in presence of excipients. Similar findings were reported in a study in their compatibility studies of antiretroviral drugs with cellulose polymers[12], [13].

HPMC (Hydroxypropyl methylcellulose) is a widely used polymer in sustained release formulations due to its excellent gelling and matrix forming properties. Both K4M and K100M grades of HPMC are non-ionic cellulose ethers that form viscous solutions and are compatible with most drugs[13], [22]. The compatibility observed in our study supports their selection for developing gastroretentive microspheres of Abacavir sulphate. According to Prajapati et al., (2013), HPMC polymers provide pH-independent release and excellent stability in gastric environment[8].

Based on the preformulation studies, several important conclusions can be drawn for formulation development:

The poor flow properties of drug powder indicate that glidants must be incorporated in the formulation to ensure uniform mixing and processing[10].

The free solubility in water and neutral pH suggest that the drug will dissolve readily and maintain stability in gastric environment[20].

The compatibility with HPMC K4M and HPMC K100M confirms that these polymers can be safely used for developing gastroretentive microspheres[13].

The melting point of 165°C indicates that the drug can withstand normal processing temperatures without degradation[18].

The selection of appropriate polymer combination and concentration will be crucial for achieving desired floating behavior and sustained drug release. HPMC polymers of different viscosity grades can be combined to optimize the release profile and buoyancy characteristics[13]. Studies by Verma et al. demonstrated that combination of HPMC K4M and K100M in 1:1 ratio provides optimal floating properties and sustained release for 12 hours[18].

Gastroretentive drug delivery systems are designed to prolong the residence time of drug in stomach, which is beneficial for drugs with narrow absorption window in upper gastrointestinal tract. Floating microspheres are one of the approaches used for gastric retention[2], [10], [11].

Abacavir sulphate, an antiretroviral drug used in HIV treatment, requires controlled release to maintain therapeutic blood levels and reduce dosing frequency. The development of gastroretentive microspheres can offer several advantages including:

Prolonged gastric residence time

Sustained drug release

Reduced dosing frequency

Improved patient compliance

Minimized side effects[7], [8]

According to Tripathi et al., (2019), gastroretentive systems are particularly beneficial for antiretroviral drugs as they provide consistent drug levels and reduce pill burden in HIV patients. The polymer selection is critical for achieving desired floating and release characteristics. HPMC polymers swell upon contact with gastric fluid and form a gel layer around the microspheres. This gel layer controls the drug release and also contributes to buoyancy[6], [8].

The combination of different viscosity grades (K4M and K100M) can provide optimized release pattern and floating duration. According to research by Patil et al., (2016), microspheres prepared with HPMC K4M showed faster drug release while K100M provided more sustained release. The combination of both grades helps in achieving desired release kinetics[11].

The mechanism of floating involves the entrapment of air or gas within the polymer matrix, which reduces the density of microspheres below 1 gm/ml, making them buoyant in gastric fluid[2]. The use of volatile solvents like dichloromethane

during preparation helps in creating porous structure that enhances floatability[7].

Abacavir sulphate is a nucleoside reverse transcriptase inhibitor (NRTI) used in combination therapy for HIV-1 infection. The drug has good oral bioavailability but requires multiple daily dosing which affects patient compliance[23]. Development of sustained release gastroretentive formulation can address this limitation.

According to clinical studies by Kumar et al., poor adherence to antiretroviral therapy is a major cause of treatment failure in HIV patients[12]. Once-daily or twice-daily dosing through controlled release formulations can significantly improve patient compliance. The gastroretentive approach offers additional advantages as it maintains drug concentration in upper GIT where maximum absorption occurs[23].

Studies by Bera et al., (2015) showed that gastroretentive microspheres of antiretroviral drugs provided sustained plasma levels for 12-24 hours compared to conventional tablets. This extended duration can help in reducing dosing frequency and improving therapeutic outcomes.

Quality by Design Approach

Modern pharmaceutical development follows Quality by Design (QbD) principles where preformulation studies play crucial role in identifying critical quality attributes. The systematic evaluation of drug properties helps in understanding the material characteristics and their impact on formulation performance [22].

In our study, the identification of poor flow properties early in preformulation stage helps in planning appropriate manufacturing process and excipient selection. The compatibility data ensures that selected polymers will not interact with drug during storage. These findings form the basis for developing robust formulation with desired quality attributes [11].

According to Bharate et al., comprehensive preformulation studies reduce the risk of formulation failure and help in achieving product quality targets[21]. The data generated in this study provides scientific justification for excipient selection and process development.

Future Considerations

The preformulation data obtained in this study provides a strong foundation for developing gastroretentive microspheres of Abacavir sulphate. Further studies should focus on:

Optimization of polymer ratio using design of experiments approach[19]

Selection of appropriate manufacturing method like emulsion solvent evaporation or ionotropic gelation [22]

Evaluation of particle size distribution and surface morphology using SEM analysis[12]

Assessment of floating behavior including floating lag time and total floating time [11]

Drug release kinetics study in simulated gastric fluid [2]

Stability studies of final formulation as per ICH guidelines [17]

The development of gastroretentive microspheres requires careful consideration of multiple factors including polymer selection, drug-polymer ratio, particle size, and manufacturing parameters. The preformulation data serves as a guide for systematic formulation development[22].

CONCLUSION

The ultimate goal for sustained drug release is to maximize therapeutic activity while minimizing the negative side effects of the drug. In this regard, floating microspheres have emerged as a novel drug delivery system to treat HIV with Abacavir sulphate.

The type of polymer affects the drug release rate and the mechanism. Polymer swelling is crucial in determining the drug release rate and is also important for flotation. A lesser FLT and a prolonged floating duration could be achieved by using different polymer combinations.

The preformulation studies were successfully conducted for Abacavir sulphate as per standard procedures. The drug showed off-white colored powder with odorless nature. The flow properties indicated poor flowability with angle of repose 29°28", compressibility index 28.04%, and Hausner ratio 1.34, which necessitates the use of glidants in formulation. The melting point was found at 165°C confirming the purity and thermal stability of drug. The drug solution showed neutral pH of 7.5 and freely soluble nature in water, which are favorable properties for gastroretentive formulation development.

The drug-excipient compatibility studies revealed no physical or chemical interaction between Abacavir sulphate and selected excipients. The FTIR analysis confirmed the absence of any incompatibility with HPMC K4M and HPMC K100M, supporting their use in the formulation. All the preformulation parameters were found within acceptable limits and comply with pharmacopoeial specifications.

These findings suggest that Abacavir sulphate is suitable for developing gastroretentive microspheres. The compatibility with HPMC polymers supports their use in formulation development. The ultimate goal of developing sustained release gastroretentive microspheres is to maximize therapeutic activity while minimizing side effects of the drug. The polymer selection and their concentration will play important role in controlling drug release rate and floating behavior. The combination of different polymer grades can help achieve desired floating lag time and prolonged floating duration, ultimately improving patient compliance in HIV therapy

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