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Improvement of the aqueous solubility and dissolution rate of the Sesamin-Sesamolin complex by cyclodextrin complexation

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ABSTRACT
UV spectroscopy was used to examine the solubility and dissolution profiles of the Sesamin-Sesamolin complex (SSC), SSC with β-cyclodextrin (β-CD), and Hydroxypropyl-β-cyclodextrin (HP-β-CD) inclusion complexes.pH-dependent solubility study and pH-dependent stability were also performed. Phase solubility study indicated the stoichiometry molar ratio 1:1 between SSC and β-CD as well as SSC and HP-β-CD. The profile was categorized as AL type by the phase solubility diagram as well. SSC inclusion complexes with β-CD and HP-β-CD were made using physical, kneading, and slurry complexation methods. FTIR, XRD, and SEM were used to characterize the complexes. In-vitro dissolution studies of the complexes were performed, and it was found that the inclusion complexes dissolve faster than SSC. Powder flow properties of the inclusion complexes as well as the quality control tests for the filled capsules were also performed.
Keywords: Sesamin, Sesamolin, β-cyclodextrin, Hydroxypropyl-β-cyclodextrin, FT-IR, XRD, SEM, Dissolution rate

I. INTRODUCTION

Sesamin and Sesamolin are the major lignans extracted from the seeds of Sesamum indicum(Lim, 2007), belonging to the family Pedaliaceae. Enhancing hepatic chemical detoxification, reducing chemically generated tumors, protecting neuronal cells from oxidative stress, and exhibiting anti-allergic, anti-inflammatory, and anti-hypertensiveeffects are a few of the medicinal uses(Jeng, 2005). Sesamin and Sesamolin are also utilized as active components in formulations for disinfectants, bactericides, viricides, anti-tuberculous, antioxidants, and antiseptics.

Cyclodextrins are starch-derived,non-hygroscopic, cyclic, crystalline oligosaccharides. Cyclodextrins with 6, 7, and 8 glucose units, respectively, are called α-, β-, and γ-cyclodextrins(Chaudhary, 2012). Cyclodextrin hasan outer hydrophilic moiety and an inner lipophilic cavity(Rasheed, 2008).Cyclodextrins are utilized as a complexing agent to improve the solubility, bioavailability, and stability of poorly aqueous soluble drug compounds(Carneiro, 2019). Cyclodextrin molecules have a cone-like form, with primary groups extending from the narrow edge and secondary hydroxyl groups from the wider edge(Kumar, 2013).

In this research, a pH-dependent solubility study and a pH-dependent stability study were conducted. Phase solubility investigations were carried out to establish the stoichiometric ratio of SSC and the complexing agents β-cyclodextrin and hydroxypropyl-β-cyclodextrin. The data was also used to establish the stability constant of the complexes. SSC inclusion complexes with β-CD and HP-β-CD were made using physical, kneading, and slurry complexation methods. Characterization of SSC and inclusion complexes were done using saturation solubility study, IR spectral analysis, scanning electron microscopy, and XRD analysis. SSC and inclusion complex's dissolution rates were investigated and contrasted.

By using the bulk density and tapped density, angle of repose, Hausner's ratio, and compressibility index methodologies, the evaluation of powder flow characteristics was completed. The inclusion complexes were filled into empty hard gelatin capsules (size 2) and quality control tests were performed.

II. MATERIALS AND METHODS

2.1 Materials

Sesamin-Sesamolin complex was procured from Sami Labs Ltd., Telangana, India. Gangwal Chemicals Pvt. Ltd., Mumbai, India, and Signet Chemical Corporation Pvt. Ltd., Mumbai, India provided β-CD and HP-β-CD as gift samples.All other materials were of analytical reagent grade.

2.2 Standard calibration curve

Calibration curve of SSC was constructed separately using water, 0.1N Hydrochloric acidand Phosphate buffer (pH 6.8) for estimation of SSC.A set of dilutions were created from the stock solution

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of SSC (100 µg/mL) by withdrawing required concentration of SSC and diluting it to 10.0 mL with respective medium so as to attain in the absorbance range of 0.1-1.3.

2.3 pH dependent solubility studies

SSC's pH-dependent solubility in distilled water, 0.1N Hydrochloric acid, and Phosphate buffer (pH 6.8) was studied. Using a 25.0 mL volumetric flask, excess SSC was added to each of the medium's 25.0 mL of volume. These flasks were then shaken. The flasks were allowed to stand for 10 minutes and from this 10.0 mL of the supernatant was withdrawn and centrifuged for 10 minutes at 2500 rpm. With the aid of the equation discovered from the standard calibration plot in each individual medium, the concentration was calculated.

2.4 pH dependent stability studies

The working standard solution of the SSC of 10.0 µg/mL was prepared by pipetting out 1 mL of the stock solution of 100 µg/mL in each of the four volumetric flasks and diluting it up to the mark with distilled water, 0.1N Hydrochloric acid and Phosphate buffer (pH 6.8) respectively. At 0, 2, 4, and 6 hours, the spectra of these dilutions were collected using a UV-Visible spectrophotometer in the 200-400 nm scanning range.

2.5 Phase solubility analysis of SSC

Phase solubility tests were carried out to establish the stoichiometric ratio of SSC and the complexing agents β-cyclodextrin and Hydroxypropyl-β-cyclodextrin. The data was also used to establish the stability constant of the complexes(Priya, 2018). Stock solutions of 10 mM of β-CD and HP-β-CD were created for this purpose using distilled water. These stock solutions were properly diluted with distilled water to produce molar solutions in 25 mL volumetric flasks for both β-cyclodextrin and Hydroxypropyl-β-cyclodextrin that ranged from 2 mM to 10 mM. The excess SSC (25 mg) was then added to each flask separately after the solutions had been transferred to 100 mL conical flasks. The flasks were shaken using a rotary shaker at 100 rpm for 24 hours at room temperature. The supernatant solutions (10 mL) were carefully collected and centrifuged at 2500 rpm for 10 minutes. Following the proper dilution of the solutions, the UV absorbance of the resulting solutions was measured at 235 nm and used to calculate the SSC concentration.

2.6 Preparing inclusion complexes

Slurry complexation, physical mixing, and the kneading method were used to create inclusion complexes of SSC with β-CD and HP-β-CD. For the physical mixture approach, the necessary molar (1:1) amounts of SSC, β-CD and HP-β-CD were precisely weighed and vigorously mixed in an agate mortar with vigorous trituration for approximately two hours. These mixes were pounded into a fine powder and then put away until later usage in sealed containers(Mendes, 2016). The necessary amounts of SSC, β-CD and HP-β-CD, for the kneading process were precisely weighed in molar ratio (1:1). The cyclodextrin and SSC were combined into a homogenous paste in the mortar by gradually adding a water/ethanol combination (1:1 v/v) and kneading continuously for two hours. To keep the paste at the proper consistency, a suitable amount of water/ethanol mixture (1:1 v/v) was added to the mortar. The paste was dried at 50°C in a hot air oven. The dried compound was then ground into a powder in an agate mortar and kept until use in sealed containers(Patel, 2007). For the slurry complexation procedure, the necessary amount of SSC, CD, and HP-CD (1:1 molar ratio) were precisely weighed and mixed in 10 mL water using a mechanical stirrer at 400 rpm for 36 hours. The mixture was then dried in a hot air oven at 50 °C. The dried compound was then ground into a powder in an agate mortar and kept until use in sealed containers(Menezes P. P., 2013).

2.7 Characterization of SSC inclusion complex

Saturation solubility analysis, Scanning Electron Microscopy (SEM), IR spectral analysis, and X-Ray Diffractometry analysis were used to characterise SSC inclusion complexes.200 mg of each compound was introduced to a 100 mL conical flask holding 25 mL of water for the saturation solubility study.Following that, the flasks were maintained at room temperature on a rotary shaker for 24 hours at 100 rpm. Also retained with the other complexes as a control was pure SSC in an equal proportion.The flasks were then let to stand for 10 minutes, after which 10 mL of the supernatant was removed and centrifuged at 2500 rpm for 10 minutes.The solutions were properly diluted, and using the equation derived from the standard calibration plot, the concentration was measured(Deshmukh, 2010). Inclusion complexes were analysed using Shimadzu Attenuated Total Reflection-Fourier Transform Infrared Spectrophotometer.SEM was

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employed to analyse the inclusion complexes. Analysis was carried out using Carl-Zeiss Scanning Electron Microscope.

2.8 In vitro dissolution study

Inclusion complexes containing 50 mg of SSC were measured out and placed in gelatin capsules.50 mg of pure SSC was used as a control, in similar manner. Dissolution study was carried out using Dissolution apparatus I.As a dissolution medium, 900 mL of distilled water was employed.The baskets were rotated at a 50 rpm pace. The medium's temperature was kept at 37°C±0.5°C. At intervals of 10, 20, 30, 40, 50, and 60 minutes, aliquots (5 mL) were taken out and 5 mL of new dissolving media was added.Samples were filtered using paper with a 0.22 µm pore size. At 235 nm, the absorbances were measured, and the % cumulative drug releasewas computed.

2.9 Evaluation of powder flow properties

By calculating bulk density and tapped density, Hausner's ratio, compressibility index, and angle of repose, powder flow characteristics were evaluated. 2 gm of each inclusion complex's powder were weighed and run through sieve number 18 to remove any potential agglomerates that may have developed during storage before being used to calculate the bulk and tapped density.The powder was then added to a graduated measuring cylinder with a 10 mL capacity. Without compacting, the powder was gently levelled, and the bulk volume was calculated.The powder sample cylinder was then manually tapped by being raised and let to fall from a height of about 2 cm. 500 taps were made on the cylinder, and the tapped volume was recorded.Utilizing the formulas below, bulk density and tapped density were computed;

Bulk density = Weight of the powder/Bulk Volume of the powder

Tapped density = Weight of the powder/Tapped volume of the powder

Using the following formula, the compressibility index of the powders was calculated;

Compressibility index (%) = [(Tapped density-Bulk density) X 100]/Tapped density

The powders' Hausner's ratio was estimated using the formula below;

Hausner’s ratio = Tapped density/Bulk density

The glass funnel technique was used to calculate the angles of repose for both powders. Powders were precisely weighed and freely flowed down the funnel to form a pile.The powder cone's diameter was measured, and the angle of repose was determined using the equation below,

$$Ø = Tan^{-} h/r$$

where the powder cone's radius and height are, respectively, r and h(Amrutha, 2017).

2.10Preparation of capsules

Manually, inclusion complexes corresponding to 50 mg of the dosage were placed inside of hard gelatin capsules (size 2).

2.11Quality control tests of capsules

Quality control tests performed were physical appearance, weight variation test, locked length and In vitro disintegration test.The capsules' outward appearance was examined during the examination of physical appearance. The capsules must have a consistent appearance.The Lab India Disintegration equipment was used to conduct the In-vitro disintegration test.The six tubes of the basket assembly each held one capsule, and discs were added to each tube to stop the capsules from floating out of the baskets.Then, this assembly was placed in a 1 L beaker that contained 900 mL of water and was kept at a temperature of 37±2°C. In order to measure how quickly the filled capsules disintegrated, the basket was then pushed up and down over a distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute.The locked or closed length of 10 capsules were recorded using vernier calliper. The locked length of size 2 capsule is 18 ± 0.3 mm.An entire capsule was weighed for the weight variation test. The capsule was then opened without damaging any of the shell, and the entire contents were taken out. Weighing was done with the empty shell. By deducting the weight of the intact capsule from the weight of the empty shell, the weight of the contents was estimated.

III. RESULTS AND DISCUSSION

3.1 Constructing a standard calibration curve

Plotting standard calibration curves in each medium, including distilled water, 0.1N Hydrochloric acid, and Phosphate buffer (pH 6.8), was done to make a quantitative estimation of SSC. **Fig. 1** shows the calibration curve,

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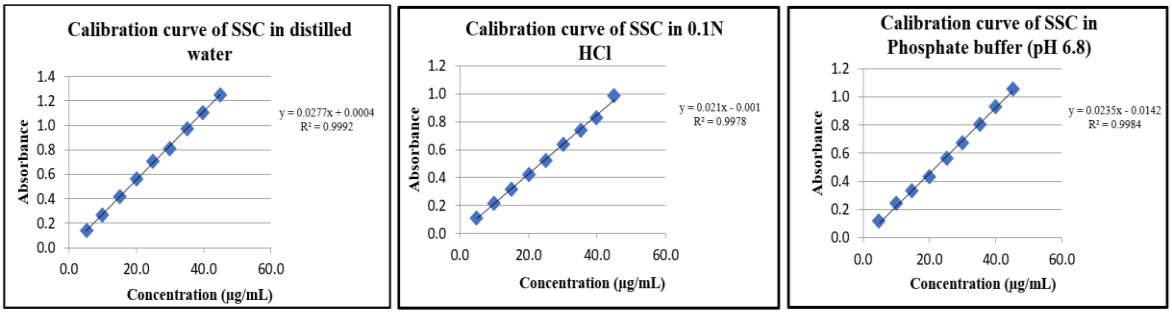

Fig. 1. Standard calibration curve of SSC in distilled water, 0.1 N Hydrochloric acid, and Phosphate buffer (pH 6.8)

3.2 pH dependent solubility study

In each media, the SSC's pH-dependent solubility was tested.The concentration was calculated using standard calibration plot equation which was obtained from the data of concentration versus absorbance prepared in the respective medium**(Fig. 2).**

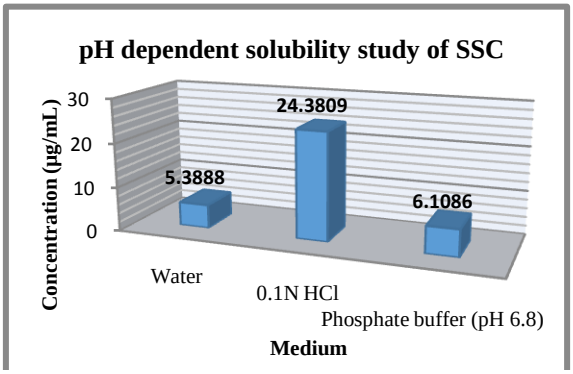

Fig. 2. pH-dependent solubility study of SSC

3.3 pH-dependent stability study

The chemical stability of SSC solution was determined in respective medium usingspectrophotometric analysis.Within the specified time frame of six hours, no notable changes in the recorded spectra were noticed. It demonstrates the SSC's stability within a given pH range.

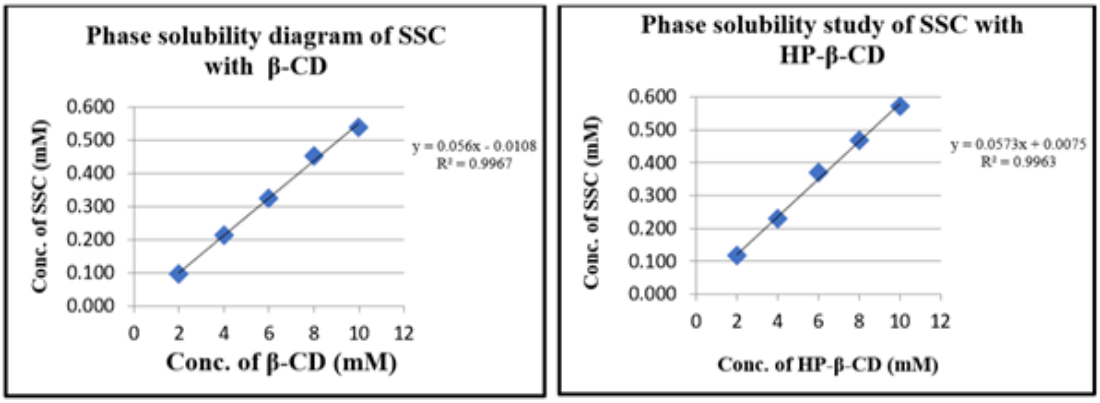

Fig. 3. Phase solubility analysis plot of SSC with β-cyclodextrin and Hydroxypropyl-β-cyclodextrin

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3.4 Phase solubility study

To estimate the stoichiometric ratio of SSC and the complexing agentsβ-cyclodextrin and Hydroxypropyl-β-cyclodextrin, phase solubility tests were performed. **Fig. 3** shows the phase solubility analysis plot for SSC with β-cyclodextrin and Hydroxypropyl-β-cyclodextrin.

The phase solubility study plots indicated that SSC solubility increased when β-cyclodextrin and Hydroxypropyl-β-cyclodextrinconcentrations increased.Both the complexes exhibited A_L type of plotand slope less than 1indicating 1:1 stoichiometry for the complexation of SSC with cyclodextrins(Kaur, 2019).

Stability constant of SSC and Cyclodextrin complexes were calculated using the following equation,

$$Kc = {}^{slope}/_{So(1-slope)}$$

where K_c = stability constant, S_0 = solubility of SSC in absence of cyclodextrin.

Slope and stability constant values were calculated as follows,

Cyclodextrin	Slope	Stability constant (M^{-})
β-CD	0.056	3645.793
HP-β-CD	0.057	3706.966

According to a report, stability constant (K_c) values between 50 and 5000 M^{-} were thought to be the most suitable for increasing the solubility and stability of compounds that weren't very water-soluble(Loh, 2016).

3.5 Characterization of SSC inclusion complexes

3.5.1 Saturation solubility study of SSC-CD complexes

200.0 mg of all complexes were added to 100.0 mL conical flasks containing 25.0 mL of water. The flasks were then kept on a rotary shaker at 100 rpm for 24 hrs at ambient temperature. Pure SSC in equivalent quantity was also kept with othercomplexes as control.The flasks were then let to stand for 10 minutes, after which 10mL of the supernatant was withdrawn and centrifuged at 2500 rpm for 10 minutes.Following the proper dilution of the solutions, the concentration was calculated using the equation derived from the standard calibration plot. **Fig. 4** shows the findings of the saturation solubility research.

Saturation solubility study results showed that, compared to pure SSC, the inclusion complexes made using all three techniques had a higher solubility. In the case of β- cyclodextrin, the complex formulated by the kneading technique showed the highest solubility whereas, in the case of Hydroxypropyl-β-cyclodextrin, the complex prepared by slurry complexation showed the highest solubility.

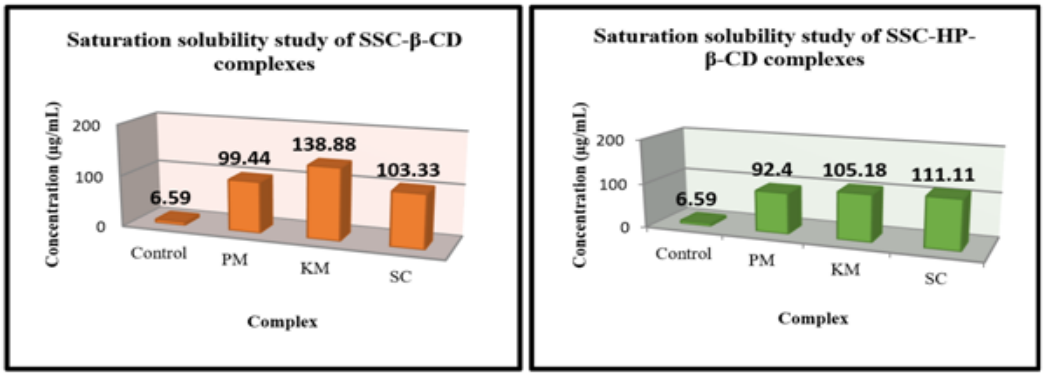

Fig. 4. Saturation solubility study of SSC-β-cyclodextrin and SSC-Hydroxypropyl-β-cyclodextrin complexes

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3.5.2 IR spectral analysis

SSC, β-cyclodextrin, Hydroxypropyl-β-cyclodextrin, SSC-β-cyclodextrincomplex prepared using kneading technique and SSC-Hydroxypropyl-β-cyclodextrincomplex prepared using slurry complexation method was analyzed using Shimadzu Attenuated Total IR spectra are depicted below, in **Fig. 5**,

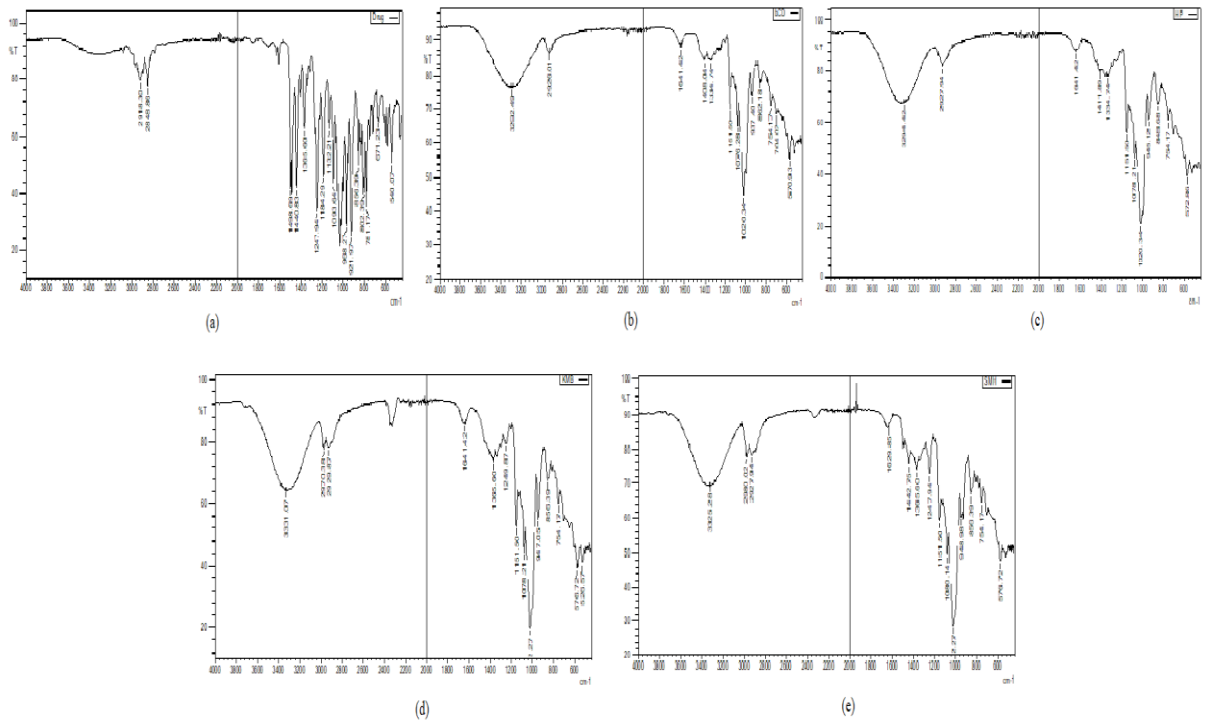

Fig. 5. IR spectra of (a) SSC, (b) β-cyclodextrin, (c) Hydroxypropyl-β-cyclodextrin, (d) SSC-β-cyclodextrin by kneading method, (e) SSC-Hydroxypropyl-β-cyclodextrin by slurry complexation method

The IR spectra of pure SSC exhibit two strong peaks at 1498.69 cm^{-1} and 1440.83 cm^{-1} that are caused by C-H bending vibrations, as well as two peaks at 2918.30 cm^{-1} and 2848.86 cm^{-1} that are caused by C-H stretch for alkenes.

O-H stretch causes a wide peak in the IR spectrum of β-cyclodextrin at 3292.49 cm^{-1}. C-H stretch vibrations of the CH_2 and C-H groups can be seen at 2926.01 cm^{-1}. O-H bending vibrations have a peak that can be noticed at 1641.42 cm^{-1}. Due to the ether and hydroxyl group bonds' C-O stretching vibrations, a noticeable peak at 1020.34 cm^{-1} can be noticed.

Similar peaks to those ofβ-cyclodextrin are visible in Hydroxypropyl-β-cyclodextrin's spectra. A large peak at 3294.42 cm^{-1} is seen as a result of O-H stretching vibrations. The peak of the C-H stretch vibrations for the CH2 and C-H groups is at 2927.94 cm^{-1}. At 1641.42 cm^{-1}, the O-H bending vibration peak may be noticed. Due to the ether and hydroxyl group bonds' C-O stretching vibrations, a strong peak at 1020.34 cm^{-1} is observed, just like inβ-cyclodextrin.

In case of IR spectra of SSC-β-cyclodextrincomplex prepared by kneading method there were noticeable changes recorded. The peak ofβ-cyclodextrin O-H stretch can be seen at 3331.07 cm^{-1}. The peak of C-H stretch for alkenes of the SSC (2918.30 cm^{-1} in pure SSC spectra) is shifted and can be seen at 2970.38 cm^{-1}. The β-CD peak of C-H stretch for alkenes at 2929.87 cm^{-1} is present. At 1641.42 cm^{-1}, the β-cyclodextrin peak caused by O-H bending vibrations can be noticed. The two distinct SSC peaks at 1498.69 cm^{-1} and 1440.83 cm^{-1} that were caused by C-H bending vibrations have vanished. The peak at 1022.27 cm^{-1}, which was caused by C-O stretching vibrations of ether and hydroxyl group bonds, is still clearly visible.

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The peak of theHydroxypropyl-β-cyclodextrinO-H stretch can be seen at 3325.28 cm^{-1} in the IR spectrum of the SSC-Hydroxypropyl-β-cyclodextrin complex produced by the slurry complex. For SSC alkenes, the peak of the C-H stretch, which appears at 2918.30 cm^{-1} in pure SSC spectra, has been moved and can now be observed at 2980.02 cm^{-1}. At 1629.85 cm^{-1}, theHydroxypropyl-β-cyclodextrin peak caused by O-H bending vibrations can be noticed. Similar to the kneading procedure utilizing β-cyclodextrin, the large SSC peaks at 1498.69 cm^{-1} and 1440.83 cm^{-1} caused by C-H bending vibrations have vanished. The peak at 1022.27 cm^{-1}, which was caused by C-O stretching vibrations of ether and hydroxyl group bonds, is still clearly visible.

It is clear from the facts above that there has been a significant molecular change, and it is possible to deduce from these observations that the hydrophobic moiety that causes the low aqueous solubility has been incorporated into the hydrophobic cavity of the cyclodextrin molecule(Menezes P. P., 2013).

3.5.3 Scanning Electron Microscopy (SEM)

SEM examination was performed using a Carl-Zeiss scanning electron microscope on pure SSC,β-cyclodextrin,Hydroxypropyl-β-cyclodextrin, SSC-β-cyclodextrincomplex, and SSC-Hydroxypropyl-β-cyclodextrincomplex**(Fig. 6).**

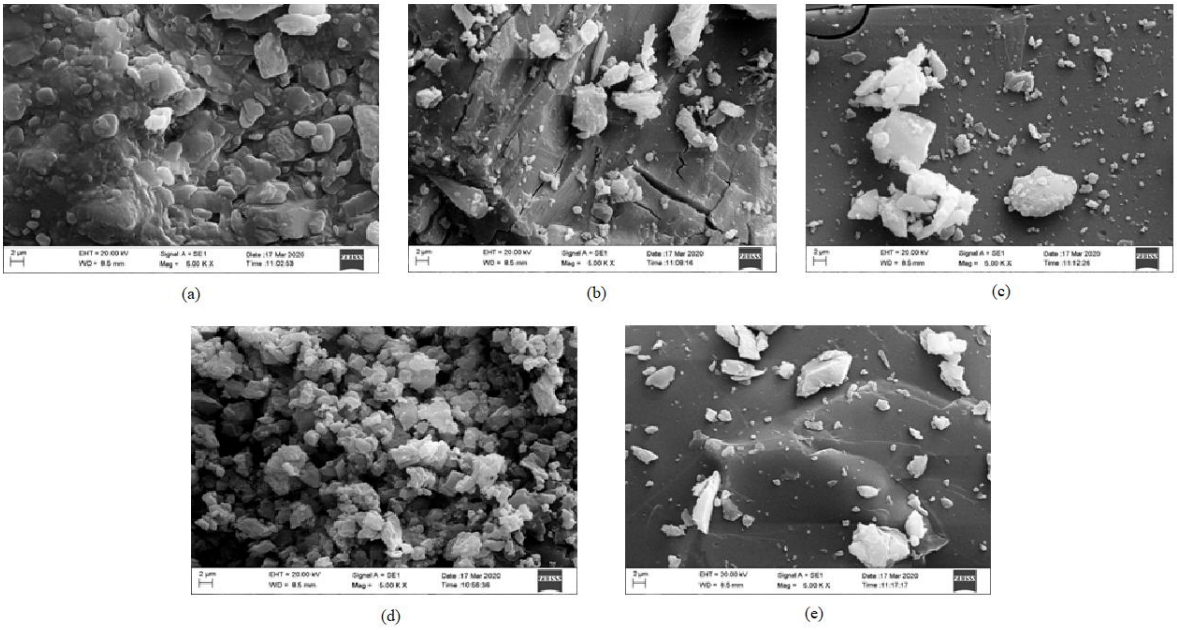

Fig. 6. SEM images of (a) SSC, (b) β-cyclodextrin, (c) Hydroxypropyl-β-cyclodextrin, (d) SSC-β-cyclodextrin by kneading method, (e) SSC-Hydroxypropyl-β-cyclodextrin by slurry complexation method

The SEM image of SSC shows spherical and oval shaped particles and not crystalline. The images ofβ-cyclodextrinand Hydroxypropyl-β-cyclodextrinwere found to be in crystalline form with sharp edges.

The SEM image of SSC-β-cyclodextrincomplex prepared using kneading technique shows change in the morphology of the particles. As compared to SEM image of pure β-CD, the particles size appears to be reduced and the particles appear as agglomerated. But the crystalline structure of the cyclodextrin is still maintained.

The crystalline structure of the cyclodextrin is still present in the SEM image of the SSC- Hydroxypropyl-β-cyclodextrin made using the slurry complexation process, and the shape of the particles did not significantly alter from the SEM image of the pure Hydroxypropyl-β-cyclodextrin. The results of the SEM analysis indicate that an inclusion complex has occurred.

3.5.4 XRD analysis

In a diffractogram, peak heights are indicators of sample crystallinity and peak position (angle of diffraction) is a sign of a crystal structure(Sinha, 2005).FromXRD analysis it was

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observed that SSC andβ-cyclodextrin were crystallinewhereas Hydroxypropyl-β-cyclodextrinappeared to be in amorphous form(Abarca, 2016). The SSC showed prominent crystalline peaks at 14.980°, 21.960° and 22.803°. β CD showed prominent sharp peaks at 12.521° and 18.808°.

The XRD diffractogram of SSC-β-cyclodextrincomplex prepared using kneading technique showed reduction in number of crystalline peaks as compared to diffractograms of SSC and β-CD. The prominent peaks at 14.950° and 22.821° were common in diffractograms of SSC and the complex but the intensities of the peaks were greatly reduced. Also, the diffractogram showed amorphous nature to some extent.

The XRD diffractogram of SSC-Hydroxypropyl-β-cyclodextrin complex prepared using slurry complexation technique showed amorphous nature with few sharp crystalline peaks at 14.954°, 21.931° and 22.817° which were prominent in diffractogram of SSC.

The XRD diffractograms of the complexes showed change in molecular organization.This shows that SSC and cyclodextrins formed an inclusion complex**(Fig. 7).**

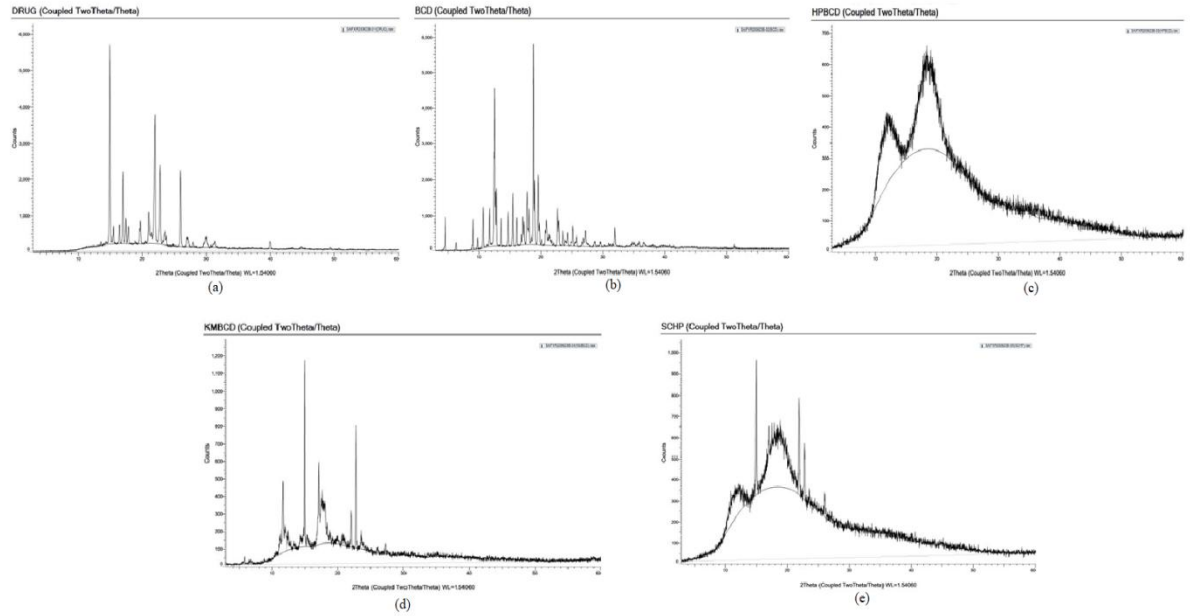

Fig. 7. XRD diffractograms of (a) SSC, (b) β-cyclodextrin, (c) Hydroxypropyl-β-cyclodextrin, (d) SSC-β-cyclodextrinby kneading method, (e) SSC-Hydroxypropyl-β-cyclodextrinby slurry complexation method

3.6 In-vitro dissolution study

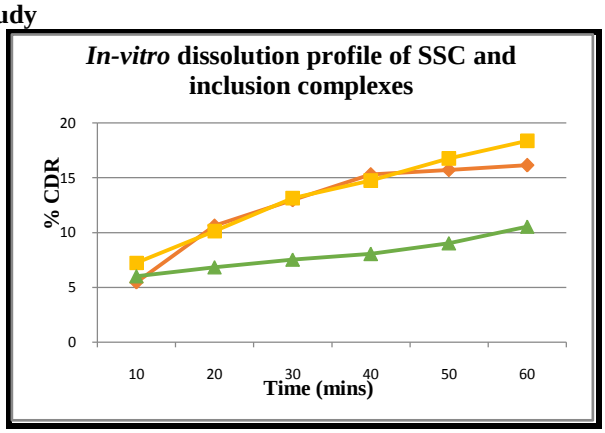

Fig. 8: In-vitro dissolution rate profile of SSC and inclusioncomplexes in water asdissolution medium, - pure Sesamin - Sesamolin complex, - SSC-β-cyclodextrincomplex using kneading technique, - SSC-Hydroxypropyl-β-cyclodextrincomplex using slurry complexation

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From above figure**(Fig. 8),** it was concluded that dissolution rate of complexes was enhanced compared to the pure SSC. The % CDR results show that the drug release ofcomplexes was better compared to pure SSC. From the results, it was concluded that formation of inclusion complex has taken place successfully.

3.7 Evaluation of powder flow properties

SSC-Hydroxypropyl-β-cyclodextrin complex using slurry complexation method and SSC-β-cyclodextrin complex using kneading technique were observed to have bulk densities of 0.400 g/mL and 0.344 g/mL, respectively.SSC-Hydroxypropyl-β-cyclodextrincomplex using slurry complexation technique and SSC-β-cyclodextrin complex using kneading technique were both found to have tapped densities of 0.526 g/mL and 0.454 g/mL, respectively.From the results, with compressibility index values between 21% - 25%, Hausner's ratio between 1.26-1.34 and angle of repose values between 30^{o} - 40^{o}, both the solid dispersions showed passable powder flow properties(Arunachalam, 2011) .

3.8 Quality control test results of capsules

3.8.1 Physical appearance

The capsules were slightly white to yellowish in colour.

3.8.2 Disintegration study

For capsules containing the SSC-Hydroxypropyl-β-cyclodextrincomplex prepared using slurry complexation technique and the SSC-β-cyclodextrin complex prepared using kneading technique, the findings of the disintegration research were determined to be 1 minute, 30 seconds and 1 minute, 28 seconds, respectively. According to the findings, the capsules' In vitro disintegration time was within acceptable limits.

3.8.3 Locked length

The study found that locked length test findings, which were 18 ± 0.3 mm, were within the acceptable range(Medisca, 2020).

3.8.4 Weight variation test

From the results, it is concluded that the weight of intact capsules and weight of inner content was equivalent to the predicted weights, i.e. weight of intact capsules for SSC-β-cyclodextrin and SSC-Hydroxypropyl-β-cyclodextrin complexes as 214.2 mg and 269.04 mg respectively and weight of inner contents as 153.2 mg and 208.04 mg respectively. Weight of the empty hard gelatin capsules were within limits i.e. 61± 4 mg (Medisca, 2020).

IV. CONCLUSION

The solubility and stability of SSC at different pH ranges i.e.distilled water, 0.1 N Hydrochloric acid, and Phosphate buffer (pH 6.8) were studied.For a period of six hours,SSC was observed to remain stable in all three pH solutions.The solubility of the SSC was found to be low in all three pH solutions but the lowest solubility was observed in distilled water.Phase solubility study of SSC in β-cyclodextrin and Hydroxypropyl-β-cyclodextrin solutions was carried out.Phase solubility profile for both the cyclodextrin showed A_L type of plot and slope less than 1 indicated 1:1 stoichiometry for complexation of SSC with cyclodextrins. The 1:1 inclusion complexes of SSC with both the cyclodextrins were developed using physical mixture, kneading and slurry complexation technique.For the complexes made using both cyclodextrins by all three techniques, a saturation solubility analysis was conducted in distilled water.From the solubility study, it was observed that SSC-β-cyclodextrin complex prepared using kneading technique and SSC-Hydroxypropyl-β-cyclodextrin complex prepared using slurry complexation technique showed highest solubility in distilled water in case of β-cyclodextrin and Hydroxypropyl-β-cyclodextrin respectively.Characterization ofSSC-β-cyclodextrin complex prepared using kneading technique and SSC-Hydroxypropyl-β-cyclodextrin complex prepared using slurry complexation technique were done by FT-IR, SEM and XRD analysis to observe change in molecular structure. Same was done for pure SSC as control sample. From the characterization, it was concluded that inclusion complexation of SSC with cyclodextrins has been achieved successfully.

The SSC-β-cyclodextrincomplex prepared using kneading technique as well as the SSC-Hydroxypropyl-β-cyclodextrincomplex prepared using slurry complexation technique had improved dissolution rates when compared to pure SSC, according to In vitro dissolution study performed using distilled water as the dissolution medium.Powder flow property evaluation techniques included bulk and tapped densities,Hausner's ratio, compressibility index, and angle of repose.Both the inclusion complexes showed passable powder flow properties.The quality control tests such as physical appearance,

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locked length, weight variation and disintegration tests for both the types of capsules were carried out. The results of quality control tests for both the types of capsules were found to be within limits.The findings indicated that the SSC-cyclodextrin inclusion complexation had been successful, increasing the Sesamin-Sesamolin complex's aqueous solubility and rate of dissolution.

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