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Enhancement Of Solubility And Dissolution Rate Of Telmisartan By Co-Crystallization Technique.

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ABSTRACT

The present study aimed to enhance the solubility and dissolution characteristics of Telmisartan, a BCS Class II drug with poor water solubility and high permeability, by preparing co-crystals using Sodium Salicylate as a co-former. The co-crystals were successfully formulated in varying drug-to-co-former ratios (1:1, 1:2, and 1:3) using both Solvent Evaporation and Liquid Assisted Grinding methods. Solubility studies of these formulations showed a significant enhancement compared to the pure drug. Among all formulations, F3 (Solvent Evaporation, 1:3 ratio) demonstrated the highest solubility (1.08 ± 0.36 mg/mL), followed by F2 and F1, indicating that increased co-former concentration favours better co-crystal formation. Liquid Assisted Grinding formulations also improved solubility, though to a lesser extent, with F6 showing the highest solubility in this group (0.884 ± 0.12 mg/mL). Drug content analysis showed acceptable ranges (95% to 100%) for all co-crystal formulations. Practical yield ranged from 90.42% to 94.16%, with F3 exhibiting the highest yield, Differential Scanning Calorimetry (DSC) analysis further confirmed the crystalline-to-amorphous transition, particularly in F3, In vitro dissolution studies revealed substantial improvement in drug release from co-crystals compared to pure Telmisartan. Pure drug released only 26.41% at 60 minutes, whereas F3 released 99.54 ±1.44%., showing a rapid and almost complete release profile. Stability studies over 3 months confirmed the physical and chemical stability of the optimized formulation (F3). Solubility, drug content, and dissolution values remained within acceptable ranges throughout the study period. The study successfully demonstrated that co-crystallization using Sodium Salicylate significantly improves the solubility, dissolution, and overall biopharmaceutical performance of Telmisartan. Among the formulations, F3 prepared by the Solvent Evaporation method with a 1:3 drug-to-co-former ratio emerged as the most promising candidate due to its superior solubility, drug content, dissolution rate, practical yield, and stability.

Keywords: Telmisartan, Liquid assisted grinding BCS Class, Co-crystals, Solubility and Dissolution.

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INTRODUCTION

The new approach available for the enhancement of drug solubility is through the application of the co-crystals, it is also referred as molecular complexes. If the solvent is an integral part of the network structure and forms at least two component crystals, then it may be termed as co-crystal. If the solvent does not participate directly in the network itself, as in open framework structures, then it are termed as Clathrate. A co-crystal may be defined as a crystalline material that consists of two or more molecular species held together by non-covalent forces. Co-crystals are more stable, particularly as the co-crystallizing agents are solids at room temperature. Only three of the co-crystallizing agents are classified as generally recognized as safe (GRAS) it includes saccharin, Nicotinamide and acetic acid limiting the pharmaceutical applications [1]. Co-crystallization between two active pharmaceutical ingredients has also been reported. This may require the use of sub therapeutic amounts of drug substances such as aspirin or acetaminophen. At least 20 have been reported to date, including caffeine and glutaric acid polymorphic co-crystals [2-3].

Co-crystallization represents a promising and increasingly popular approach for the solubility enhancement of poorly water-soluble drugs. Its ability to modify the physicochemical properties of APIs without altering their chemical structure provides a significant advantage in pharmaceutical formulation design. As regulatory agencies like the FDA and EMA increasingly recognize co-crystals as distinct solid forms, the development of pharmaceutical co-crystals is expected to grow further, paving the way for more effective and patient-friendly drug products [4].

Telmisartan is Angiotensin II Receptor Antagonist, which is used in the prevention and treatment of Hypertension. Telmisartan belongs to class II drug in BCS classification i.e. low solubility and high permeability. One of the major problems with this drug is its low solubility in biological fluids, which results into poor bioavailability after oral administration. The solubility of Telmisartan in aqueous medium was very low i.e. 0.078 mg/ml in water. Absolute bioavailability of the Telmisartan was 42-58% and biological half-life is only 24 hours that results into poor bioavailability after oral administration. Poor solubility of Telmisartan leads to poor dissolution and hence variation in bioavailability. Thus increasing aqueous solubility and dissolution of Telmisartan is of therapeutic importance [5-6].

MATERIALS AND METHODS

Materials

Telmisartan was obtained as kind gift sample from Glenmark Pharma, Goa. Sodium Salicylate & Ethanol was purchased from S.D. Fine Chem. Ltd. All other solvent and chemicals are analytical grade.

Methods

Determination of Drug Absorption Maxima (λ_{max})

The absorption maxima (λmax) of a drug refer to the specific wavelength at which a substance exhibits maximum absorbance in the UV-Visible spectrum. This wavelength is characteristic of the molecular structure of the compound and is primarily determined by the presence of chromospheres (light-absorbing functional groups). When a solution of the drug is exposed to UV or visible light, electrons in the molecule absorb energy and transition from a lower to a higher energy level. The wavelength at which this absorbance is at its peak is called λmax <, and it is used to quantitatively analyse the drug using Beer-Lambert's law.

Drug absorption maximum was determined by UV spectroscopy. Drug sample of 10 µg/ml solution was scan in the range of 200-400 nm and absorption maxima was recorded.

Saturation Solubility Study of Drug

Saturation solubility is a fundamental physicochemical property of a drug that determines its dissolution and bioavailability. It refers to the maximum amount of a solute (drug) that can dissolve in a given solvent at a specific temperature and pressure, reaching equilibrium between the dissolved and undissolved drug. Solubility is a crucial parameter in pharmaceutical sciences as it directly influences the

drug's absorption, therapeutic efficacy, and formulation design. Poorly soluble drugs often exhibit low bioavailability, making solubility enhancement strategies essential for effective drug delivery [7].

Saturation solubility study of drugs Telmisartan was tested in three solvents like distilled water, 0.1 N Hcl and phosphate buffer pH 6.8 the saturation solubility of a selected drug was determined as per Higuchi and Connor's method. Excess amount of drug was taken and added in 30 ml of solvent in a glass vial. Samples were then shaken for 48 hr. at a constant speed on a rotary shaker at 25°±C2°C. After that, the saturated solutions were filtered through a 0.45 µg millipore filter. Filtrates were diluted appropriately and concentration of drug was determined using UV spectrophotometrically [8].

Preparation of Co-crystals of Telmisartan

Two different methods were employed to prepare co-crystals of Telmisartan using sodium salicylate as conformer as described below

Preparation of Co-crystals of Telmisartan by Solvent Evaporation Method

Telmisartan and sodium salicylate were carefully weighed at different stoichiometric ratio (1:1, 1:2, and 1:3) as shown in Table 6.3. Each compound was dissolved in ethanol separately. The two solutions were mixed and sonicated for a few minutes, and then the solution of both components was poured into a Petri dish. The prepared solution was allowed to evaporate at room temperature until the solution is completely dry. The obtained co-crystal solids were stored in a tightly closed container for further evaluation [9, 10].

Preparation of Co-crystals of Telmisartan by Liquid Assisted Grinding

Liquid assisted grinding technique was used to prepare co-crystals of Telmisartan using sodium salicylate as co-former. The formation of Telmisartan co-crystals was performed in the same molar ratio (1:1, 1:2, and 1:3) as shown in Table 1. Grinding of a mixture of Telmisartan and sodium salicylate was carried out in mortar and pestle for 30 minutes with the addition of small amount ethanol drop wise 5 ml so as to get wet mass, and then the wet crystals were dried in an oven and stored for further analyses [11, 12].

Table 1: Composition of Telmisartan Sodium Salicylate Co-crystals.

Batch Code	Telmisartan: Sodium salicylate Ratio	Co-Crystallization Method
F1	1:1	Solvent Evaporation
F2	1:2	Solvent Evaporation
F3	1:3	Solvent Evaporation
F4	1:1	Liquid Assisted Grinding
F5	1:2	Liquid Assisted Grinding
F6	1:3	Liquid Assisted Grinding

In-Vitro Evaluation of Telmisartan Co-crystals.

Determination of Solubility

Solubility study of obtained co-crystals of Telmisartan prepared by different methods was performed using shake flask method. The solubility was determined in distilled water as a solvent. Excess quantities of sample were added in 20 ml of study solvent in conical flask and shaken for 24 hours at room temperature on rotary flask shaker. After shaking resultant samples filtered using Whatman filter paper. Further sample ware suitably diluted and analysed by UV- Spectrophotometer at 296 nm [13, 14].

Determination of Drug Content

Drug content of Telmisartan in the prepared co-crystals was analyzed. A weight amount of co-crystals equivalent to 40 mg of Telmisartan was carefully weighed and dissolved in ethanol in 50 mL

volumetric flask. The solutions were agitated for 30 min before being filtered through Whatman filter paper 1. The solution was then diluted properly and analyzed for drug concentration with a UV-visible spectrophotometer at 296 against blank. The analysis was carried out three times [15]

Percentage Practical Yield

Percentage practical yield was calculated to know about percent yield or efficiency of any method, thus its help in selection of appropriate method of production. Formulated co-crystals was collected and weighed to determine practical yield (PY) from the following equation [16].

$$\% \text{ Practical Yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} x\ 100$$

Fourier Transform Infra-Red Spectroscopy (FTIR)

Fourier Transform Infrared (FTIR) Spectroscopy is a widely used analytical technique for identifying the functional groups and molecular interactions in pharmaceutical substances. It works by measuring the absorption of infrared radiation by the sample at different wavelengths, producing a spectrum that reflects the molecular fingerprint of the compound. In compatibility studies, FTIR is employed to assess possible chemical interactions between a drug and excipients by comparing the characteristic peaks of pure drug, individual excipients, and their physical mixtures or formulations. If the characteristic peaks of the drug (e.g., N–H, C=O, O–H, etc.) remain unchanged in the mixture, it indicates no chemical interaction, confirming compatibility. However, any significant shift, disappearance, or formation of new peaks may suggest potential intermolecular interactions or incompatibilities [17].

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) is a thermo-analytical technique used to measure the heat flow associated with physical and chemical transitions of a substance as a function of temperature. It is a valuable tool in pharmaceutical analysis, especially for assessing the crystallinity of drug substances.

In crystalline materials, DSC typically shows a sharp and well-defined endothermic peak corresponding to the melting point, which reflects the presence of an ordered crystal lattice. In contrast, amorphous substances display a broad transition known as the glass transition temperature (Tg), and lack a clear melting point. By analysing the melting behaviour and enthalpy of fusion (ΔH), DSC can differentiate between crystalline and amorphous forms and estimate the degree of crystallinity. It also helps identify polymorphic transitions, degradation, and interactions between drug and excipients. Studying crystallinity is crucial because it directly influences the solubility, dissolution rate, stability, and bioavailability of drugs. DSC thus plays an essential role in formulation development, quality control, and stability studies [18]

In Vitro Drug Dissolution Study

In vitro drug dissolution study for pure Telmisartan and co-crystals were determined using USP paddle apparatus by dispersed powder technique. USP II dissolution equipment with a paddle stirrer was utilized for the study. Study was performed in 0.1N Hcl. Sample equivalent to 40 mg of Telmisartan was added to 900 ml dissolution medium at 37 ± 0.5°C and stirred at 50 rpm (Elctrolab). At predetermined intervals, samples of the 5 mL dissolving medium were removed and replaced with fresh samples of the same volume. The samples' drug content was examined using an absorbance measurement at 296 nm. The mean of at least three determinations was used to calculate the drug release.

Stability Studies

Stability studies was carried out on optimized formulations as per ICH guidelines by keeping the formulation sample at 40°C ± 2°C/75% RH ± 5% RH for 3 months. The optimized co-crystal formulation was stored in stability chamber (Remi, India) at 40^0 C and 75% RH for 3 months. Periodically samples were withdrawn and estimated for the drug content, solubility and in vitro drug dissolution study.

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RESULTS AND DISCUSSION

UV-Spectroscopy (Determination of λ max)

Drug absorption maximum was determined by UV spectroscopy, after scanning the solution of drug in the range of 200-400 nm and absorption maxima was recorded The lambda max (λmax) of Telmisartan was found to be 296 nm.

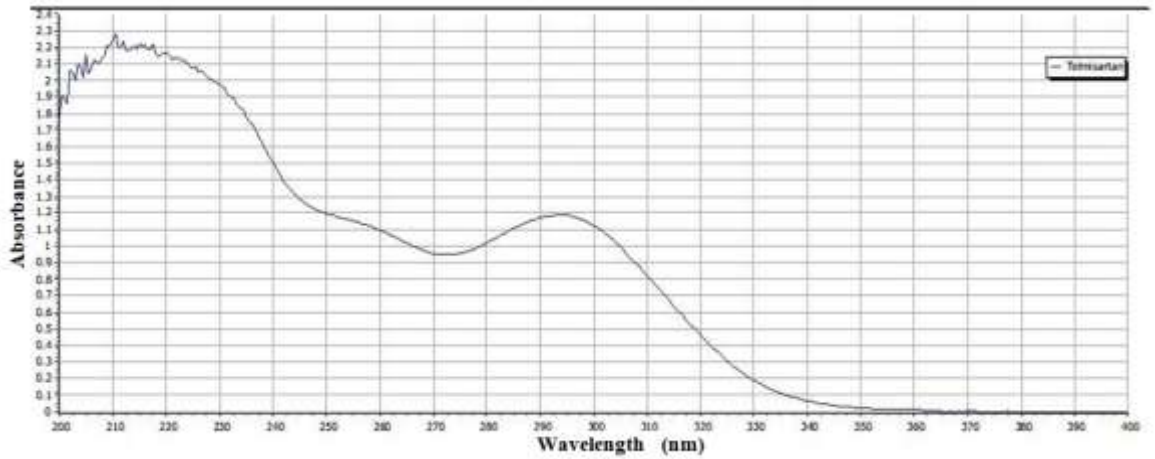

Figure 1: Absorption Maxima (λmax) of Telmisartan at 296 nm

Saturation Solubility Study of Drug Telmisartan

Saturation solubility of drug Telmisartan was studied in different solvent like and distilled water, 0.1 N Hcl, Phosphate buffer pH 6.8 and Phosphate buffer pH 7.4. The solubility study reveals that Telmisartan exhibits poor aqueous solubility in all tested media, confirming its classification as a BCS Class II drug (low solubility, high permeability). The solubility in distilled water was found to be extremely low (0.034 ± 0.054 µg/mL), indicating its practically insoluble nature in neutral pH environments. The highest solubility was observed in 0.1 N HCl (0.64 ± 0.24 µg/mL), suggesting that Telmisartan solubility improves under acidic conditions. This can be attributed to the weakly acidic nature of Telmisartan (pKa ~4.5), which remains largely in unionized form in neutral and basic media, but may exhibit slightly better solubility due to protonation in acidic pH. In phosphate buffer pH 6.8 and pH 7.5, the solubility was relatively low (0.21 ± 0.12 µg/mL and 0.28 ± 0.082 µg/mL respectively), showing a slight improvement at pH 7.5, but still indicating poor dissolution in the intestinal environment, where absorption primarily occurs. These findings emphasize the need for solubility enhancement strategies, such as co-crystals, to improve the bioavailability of Telmisartan. Solubility data of Telmisartan in different solvents are shown in table 2.

Table 2: Solubility of Telmisartan in Different Solvents

Sr. No	Solvents	Solubility (mg/ml)
1	Water	0.034 ± 0.054
2	0.1 N Hcl	0.64 ± 0.24
3	Phosphate buffer pH 6.8	0.21 ± 0.12
4	Phosphate buffer pH 7.5	0.28 ± 0.082

Characterization of Telmisartan Co-crystals.

Determination of Solubility

The solubility of pure Telmisartan and its co-crystals with sodium salicylate prepared by three different co-crystallization methods Solvent Evaporation, and Liquid Assisted Grinding was evaluated in distilled water using the shake flask technique. The solubility of pure Telmisartan in distilled water was found to be 0.034 ± 0.054 mg/mL, indicating its very poor aqueous solubility, consistent with its BCS

Class II classification. To improve its solubility, Telmisartan was co-crystallized with Sodium Salicylate using two different methods: Solvent Evaporation and Liquid Assisted Grinding (LAG), in varying molar ratios (1:1, 1:2, and 1:3).

The results revealed a significant improvement in solubility across all co-crystal formulations compared to the pure drug. Among the formulations prepared by Solvent Evaporation, solubility increased progressively with increasing the amount of co-former. Batch F1 (1:1 ratio) showed a solubility of 0.681 ± 0.18 mg/mL, batch F2 (1:2 ratio) showed 0.931 ± 0.22 mg/mL, while batch F3 (1:3 ratio) exhibited the highest solubility of 1.08 ± 0.36 mg/ml. This trend indicates that a higher concentration of sodium salicylate promotes better co-crystal formation, which leads to improved molecular interaction and lattice disruption, thereby enhancing solubility. In contrast, co-crystals prepared via Liquid Assisted Grinding also showed improved solubility, though to a lesser extent compared to solvent evaporation, batch F4 (1:1 ratio) had a solubility of 0.544 ± 0.21 mg/mL, batch F5 (1:2 ratio) was 0.714 ± 0.18 mg/mL, and batch F6 (1:3 ratio) reached 0.884 ± 0.12 mg/ml. While LAG is a simpler and solvent-free technique, it may not provide the same degree of crystallinity and molecular interaction as the solvent-based method, which could explain the comparatively lower solubility values.

Overall, the study confirms that co-crystallization significantly enhances the solubility of Telmisartan, with the Solvent Evaporation method and higher co-former ratios (especially F3) being the most effective. This enhancement is attributed to the formation of new crystalline phases with improved hydrophilicity and reduced lattice energy, facilitating better dissolution in aqueous media. Solubility study data for pure Telmisartan, its co-crystals formulations are shown in table 3.

Table: 3: Solubility Study of Pure and Co-Crystal of Telmisartan in Distilled Water.

Formulation Code	Solubility (mg/ml)	Co-Crystallization Method
Pure Telmisartan	0.034 ± 0.054	-
F1	0.681±0.18	Solvent Evaporation
F2	0.931±0.22	Solvent Evaporation
F3	1.08±0.36	Solvent Evaporation
F4	0.544±0.21	Liquid Assisted Grinding
F5	0.714±0.18	Liquid Assisted Grinding
F6	0.884±0.12	Liquid Assisted Grinding

Mean ± SD, n=3

Determination of Drug Content

The percentage drug content of Telmisartan co-crystals (F1 to F6) was evaluated to ensure uniformity and efficiency of the co-crystallization process. The results are summarized below in table 4. All the formulations exhibited drug content in the acceptable range of 95–100%, indicating that the co-crystallization process was efficient and did not lead to significant drug loss or degradation during formulation.

Among the solvent evaporation method formulations, F3 (1:3 ratio) showed the highest drug content (99.56 ± 1.12%), suggesting better entrapment or incorporation of the drug within the co-crystal matrix due to higher availability of the co-former. Similarly, F6 (prepared by Liquid Assisted Grinding with a 1:3 ratio) also exhibited high drug content (98.34 ± 1.10%), supporting the idea that increased co-former ratio contributes to enhanced drug incorporation. The slight variations in drug content among batches could be attributed to differences in mixing efficiency, particle adherence, and method of preparation. The solvent evaporation method showed slightly higher and more consistent drug content compared to the LAG method, possibly due to better control over crystal formation and drug distribution in the solvent medium.

Overall, the study confirms that both co-crystallization methods solvent evaporation and liquid-assisted grinding were effective in producing co-crystals with uniform and satisfactory drug content, with F3 and F6 being the most promising formulations.

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Table 4: % Drug Content of Telmisartan Co-Crystal (F1 to F6)

Sr. No	Formulation	% Drug Content
1	F1	96.21 ± 0.55
2	F2	97.18± 0.71
3	F3	99.56± 1.12
4	F4	97.26± 0.52
5	F5	96.67± 0.84
6	F6	98.34± 1.10

Mean ± SD, n=3

Percentage Practical Yield

All the formulations exhibited high practical yields ranging from 90.42% to 94.16%, indicating minimal loss during the preparation process and good reproducibility. Among the formulations, F3 (1:3 ratio, Solvent Evaporation method) showed the highest yield (94.16%), which may be attributed to better handling, higher crystallization efficiency, and optimal interaction between Telmisartan and the co-former Sodium Salicylate. This also aligns with its high drug content and solubility, making F3 a promising formulation overall. Formulations prepared via Solvent Evaporation (F1–F3) showed slightly higher yields than those prepared using Liquid Assisted Grinding (F4–F6). This could be due to better control over crystal growth and reduced material loss during solvent removal, whereas in grinding methods, some material loss is common due to sticking, spillage, or handling inefficiencies.

Overall, the study confirms that the co-crystallization methods employed were efficient, with minimal material wastage and good process reproducibility. These findings support the scalability and feasibility of both methods for further development. The results are given in table 5.

Table 5: Practical Yield of Telmisartan Co-Crystal Formulations (F1 to F6)

Sr. No	Formulation	% Practical Yield
1	F1	91.34
2	F2	93.42
3	F3	94.16
4	F4	92.43
5	F5	93.36
6	F6	90.42

Mean ± SD, n=3

Drug Excipients Compatibility Study

FTIR (Fourier Transform Infrared Spectroscopy) analysis was carried out to evaluate any potential chemical interaction between Telmisartan and the polymer/excipient used in the solid dispersion. The major characteristic peaks of functional groups in pure Telmisartan and its co-crystals were analysed and compared.

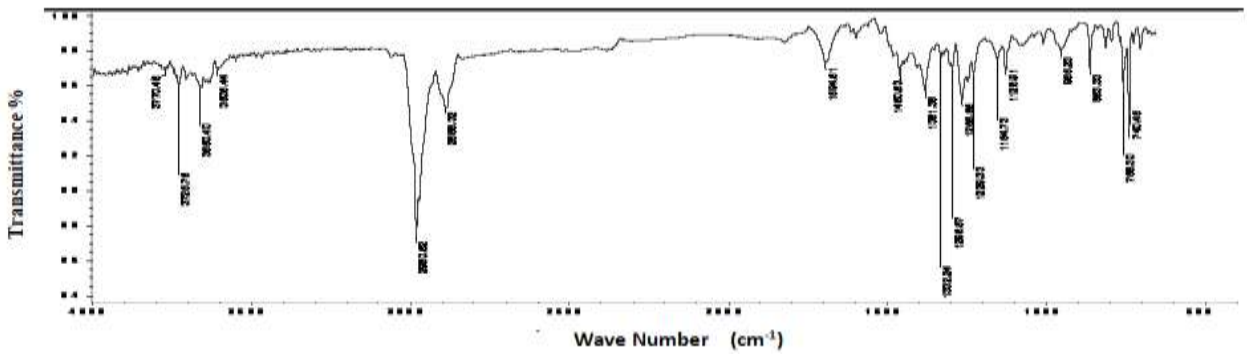

Figure 2: FTIR Spectra of Pure Telmisartan

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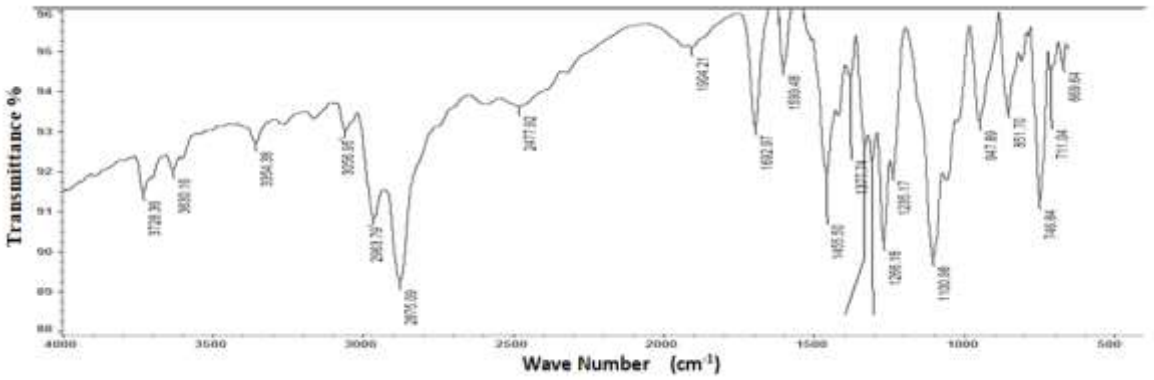

Figure 3: FTIR Spectra of Telmisartan Co-Crystals

The FTIR spectrum of Telmisartan (figure 2) shows distinct peaks that confirm the presence of its characteristic functional groups. Broad peaks observed at 3770.47 cm^{-1} and 3727.86 cm^{-1} correspond to the stretching vibrations of free hydroxyl groups (–OH), likely associated with the benzimidazole ring or carboxylic acid moiety. Additional bands at 3660.40 cm^{-1} and 3605.44 cm^{-1} may indicate N–H or hydrogen-bonded –OH stretching, suggesting possible intra- or intermolecular hydrogen bonding. Peaks at 2980.62 cm^{-1} and 2900.16 cm^{-1} are attributed to aliphatic C–H stretching, consistent with the alkyl chains in the molecule. A strong absorption band at 1694.5 cm^{-1} corresponds to the carbonyl (C=O) stretching vibration, indicative of a carboxylic acid group. Peaks at 1608.54 cm^{-1} and 1506.59 cm^{-1} represent C=C or C=N stretching vibrations, confirming the presence of aromatic and heteroaromatic structures, particularly the benzimidazole ring. Bands at 1322.2 cm^{-1} and 1256.67 cm^{-1} correspond to C–O stretching vibrations, while the peak at 1224.53 cm^{-1} is attributed to C–N stretching, further confirming the presence of aromatic amines. Additional peaks at 1164.57 cm^{-1} and 1126.91 cm^{-1} could be related to ether (C–O–C) or sulfone group vibrations. The region between 938.30 cm^{-1} and 720.45 cm^{-1} shows peaks associated with aromatic C–H out-of-plane bending, and the band at 753.30 cm^{-1} is characteristic of substituted aromatic rings. Overall, the FTIR spectrum confirms the presence of all major functional groups in Telmisartan, supporting its structural integrity and purity.

FTIR spectra of co-crystals of Telmisartan (figure 3) confirm that characteristic distinct peaks are present and detectable in spectra of FTIR of co-crystals, which confirmed that Telmisartan was chemically compatible with the components used in the co-crystallization. There was no evidence of new peak formation or significant peak shifting, indicating no chemical interaction between the drug and excipients. The physical interactions present may aid in the improved solubility or dispersion of the drug.

Differential Scanning Calorimetry (DSC)

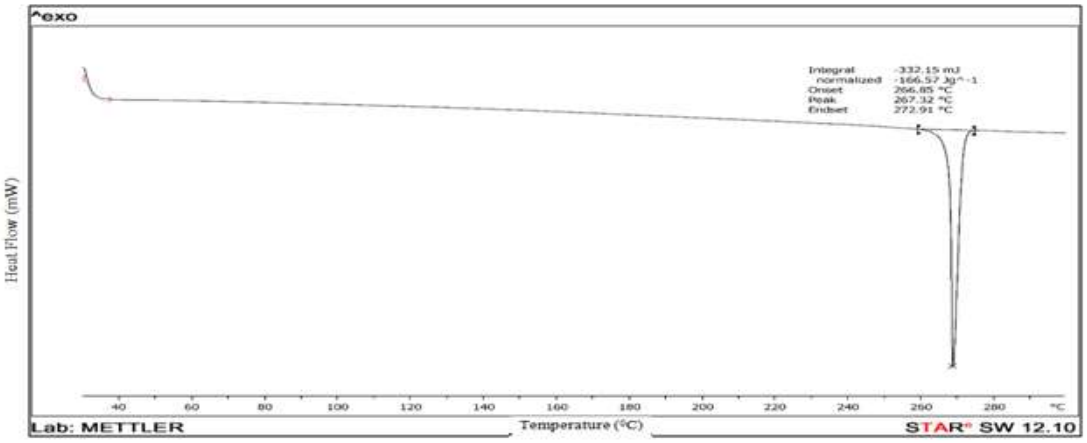

Figure 4: DCS Thermogram of Pure Telmisartan

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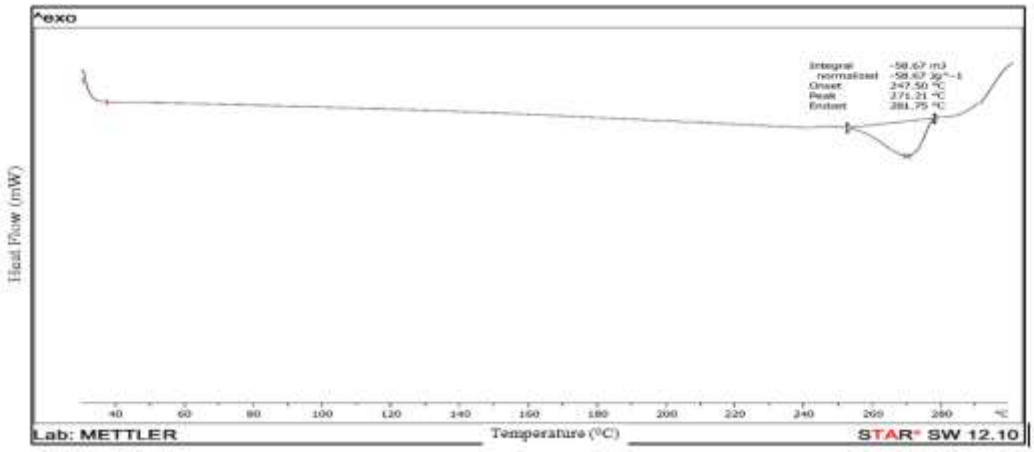

Figure 5: DCS Thermogram of Co-Crystals of Telmisartan (F3)

The DSC Thermogram of pure Telmisartan (figure 4) showed a sharp single endothermic peak at 267.32°C corresponds to the melting temperature of Telmisartan, the sharpness of the peak confirmed the crystalline nature of the Telmisartan. From the DSC study it was observed that the drug is highly crystalline in nature. Figure 5 shows the DSC thermogram of optimized Telmisartan co-crystals formulation (F3), showed less intense broader endothermic peaks at slight shifted position of 271.21°C corresponds to the endothermic peak of drug. This reduction in sharpness of peak and broadening of endothermic peak of drug indicate the amorphous conversion of crystalline Telmisartan in the presence of sodium salicylate by the process of co-crystallization.

In Vitro Dissolution Study

An in vitro dissolution study was conducted for pure Telmisartan and its co-crystals (F1–F6) prepared using solvent evaporation, and liquid-assisted grinding methods with varying drug-to-sodium salicylate ratios (1:1, 1:2, 1:3). The study aimed to evaluate the effect of co-crystallization method and co-former ratio on the drug release profile. The results are shown figure 6.

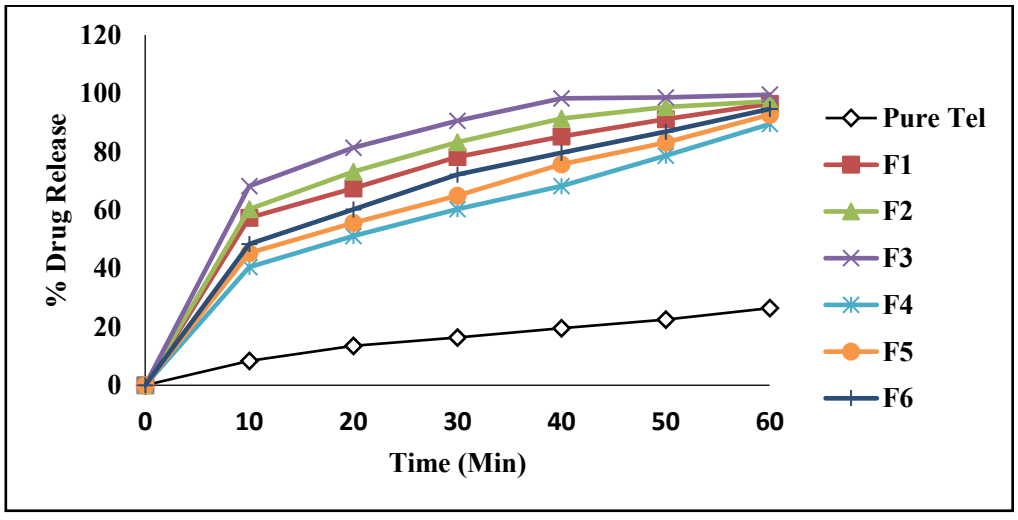

Figure 6: Dissolution Profile of Pure and Co-Crystal of Telmisartan.

The in vitro dissolution study was conducted to evaluate the drug release behaviour of pure Telmisartan and its co-crystal formulations (F1–F6) in distilled water over a 60-minute period. The results clearly demonstrate a significant enhancement in the dissolution rate of Telmisartan when formulated as co-crystals with Sodium Salicylate. Pure Telmisartan exhibited very poor dissolution, with only 26.41 ± 2.18% drug releases at the end of 60 minutes. In contrast, all co-crystal formulations showed

markedly improved drug release, indicating enhanced solubility and dissolution properties due to co-crystallization. Among the solvent evaporation method formulations, F3 (1:3 ratio) exhibited the highest dissolution, with 68.24 ± 1.26% at 10 minutes and 99.54 ± 1.44% at 60 minutes, suggesting nearly complete drug release. F2 (1:2 ratio) and F1 (1:1 ratio) also showed rapid and high dissolution, reaching 97.26 ± 2.04% and 96.44 ± 1.25% at 60 minutes, respectively. This trend indicates that increasing the co-former concentration enhances the solubilisation potential, likely due to better molecular dispersion and hydrogen bonding in the co-crystal matrix. The results clearly demonstrate that co-crystallization significantly improves the dissolution rate of Telmisartan, with the solvent evaporation method and higher drug-to-co-former ratios yielding the most effective results. This enhancement can be attributed to the modification of the drug's crystalline structure, leading to improved wettability, reduced lattice energy, and better drug–solvent interaction.

Stability Studies

The initial solubility of F3 was 1.08 ± 0.36 mg/mL, which slightly decreased to 1.02 ± 0.27 mg/mL at 1 month and 0.98 ± 0.75 mg/mL at 2 months. However, the solubility recovered slightly to 1.02 ± 0.44 mg/mL by the 3rd month. The changes observed were minor and within acceptable limits, indicating that the formulation retained its solubility-enhancing properties during storage. At the beginning of the study, the drug content was 99.56 ± 1.12%, which gradually declined to 98.16 ± 0.34% at 1 month, 96.45 ± 0.44% at 2 months, and 97.21 ± 0.34% at 3 months. Although a slight reduction was observed over time, the values remained within pharmaceutically acceptable limits (typically 90–110%), confirming good chemical stability of the drug in the co-crystal form.

The percentage drug release also remained consistent throughout the study. Initially, the formulation showed 99.54 ± 1.44% drug releases, which slightly decreased to 97.45 ± 1.67% at 1 month, 98.30 ± 1.13% at 2 months, and 98.12 ± 1.23% at 3 months. These results indicate that the formulation maintained excellent release characteristics even after 3 months of storage.

Table 6: Stability Study Optimized Telmisartan Co-Crystal Formulation (F3)

Formulation Code	Test	Stability Period			
		0 month	1 month	2 month	3 month
F3	Solubility (mg/ml)	1.08±0.36	1.02±0.27	0.98±0.75	1.02±0.44
	Drug content (%)	99.56± 1.12	98.16±0.34	9645±0.44	97.21±0.34
	% Drug Release	99.54±1.44	97.45±1.67	98.30±1.13	98.12±1.23

CONCLUSION

The study successfully demonstrated that co-crystallization using Sodium Salicylate significantly improves the solubility, dissolution, and overall biopharmaceutical performance of Telmisartan. Among the formulations, F3 prepared by the Solvent Evaporation method with a 1:3 drug-to-co-former ratio emerged as the most promising candidate due to its superior solubility, drug content, dissolution rate, practical yield, and stability. These findings support co-crystallization as a viable and scalable technique for enhancing the delivery of poorly soluble drugs like Telmisartan. The optimized formulation (F3) not only offers improved performance but also maintains stability over time, supporting its potential for further development into a clinically viable oral dosage form. Future work should focus on in-vivo bioavailability studies, stability analysis, and scale-up feasibility to further explore the clinical and commercial applicability of this method.

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