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Research Article

PREPARATION AND CHARACTERIZATION OF AZILSARTAN COCRYSTALS USING AMINO ACIDS AS COFORMERS

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ABSTRACT

Objective: This study aimed to improve the solubility and dissolution of azilsartan by forming cocrystals with D-alanine.

Methods: Azilsartan-D-alanine cocrystals were prepared using a 1:2 molar ratio through the solvent evaporation technique. Cocrystal formation was confirmed through Fourier transform infrared spectroscopy (FT-IR), DSC, PXRD, and scanning electron microscope (SEM). *In vitro* dissolution was evaluated using a USP Type II paddle apparatus with 900 mL of dissolution medium maintained at 37±0.5°C.

Results: FT-IR analysis confirmed the presence of hydrogen bonding through significant shifts in the functional group peaks. The DSC analysis exhibited a sharp endothermic peak, signifying the development of a new crystalline phase, whereas PXRD results displayed unique diffraction peaks not observed in the individual drug or coformer, validating the formation of cocrystals. SEM analysis showed a morphological transformation into a homogeneous and compact structure. The cocrystals exhibited enhanced dissolution performance, achieving a 1.35-fold increase in drug release at 60 min compared to pure azilsartan.

Conclusion: The study successfully demonstrates that cocrystallization with D-alanine significantly improves the solubility and dissolution of azilsartan. This method provides an effective way to tackle solubility issues while potentially improving the oral bioavailability of drugs with poor water solubility. The study also underscores the value of amino acid-based coformers in pharmaceutical cocrystal development.

Keywords: Azilsartan, D-alanine, Cocrystal, Solubility enhancement, Dissolution rate.

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INTRODUCTION

Solubility and dissolution significantly impact how well poorly water-soluble drugs are absorbed when taken orally [1,2]. To enhance these attributes, pharmaceutical cocrystals have gained popularity. Cocrystals, formed by non-covalent bonding of an API with coformers, enhance solubility, dissolution, stability, and melting point while preserving the drug's molecular structure [3-8].

These changes occur via heteromeric and homomeric interactions between functional groups that form predictable supramolecular synthons, thus enabling the rational design of cocrystal forms [9].

Beyond enhancing pharmaceutical performance, cocrystals offer notable advantages in intellectual property extension and green chemistry compliance [10,11]. The co-crystallization process often produces minimal waste and aligns with environmentally sustainable manufacturing principles. Cocrystals can be prepared using solution-based methods [12]. In addition, advanced technologies such as hot-melt extrusion, supercritical fluid processing, sonic slurring, and ultrasound-assisted crystallization have been explored to improve scalability and efficiency. These innovative methods provide versatility in modifying drug properties for enhanced therapeutic outcomes.

The angiotensin II receptor blocker, azilsartan, is known for its antihypertensive efficacy and is chemically defined by the formula $C_{25}H_{20}N_4O_5$ and a molecular weight of 456.46 g/mol [13]. The compound has a pKa of 5.2, indicating weakly acidic characteristics, and a log p-value of approximately 2.1, reflecting moderate lipophilicity [14]. It exists in crystalline form and demonstrates stability under ambient conditions. These physicochemical properties influence its formulation strategies and therapeutic performance in oral dosage forms [15].

Several approaches have been explored to enhance azilsartan's solubility and bioavailability, including fast-dissolving tablets [16], nanoemulsions [17], nanostructured lipid carriers [18], and S-SMEDDS [19]. Cocrystals with coformers such as nicotinamide enhanced stability and dissolution [20], while solid dispersions and nanosuspensions improved drug release [21,22].

Amino acids have been identified as promising co-formers due to their zwitterionic properties and GRAS classification, which ensures a low biological hazard [23,24]. Their capacity to engage in charge-assisted hydrogen bonding through carboxyl and amino functional groups supports their suitability in azilsartan cocrystal development [25,26].

In the present study, azilsartan cocrystals were prepared using D-alanine, a GRAS amino acid featuring an amide group (Fig. 1), by the solvent evaporation method.

MATERIALS AND METHODS

Materials

Azilsartan was kindly provided as a gift sample by MSN Laboratories Pvt. Ltd., Hyderabad, India, whereas D-alanine and analytical-grade solvents such as ethanol and methanol were procured from HI Media Laboratories Pvt. Ltd., Mumbai, India.

Instrumentation

The following instruments were employed in the study: Fourier transform infrared spectroscopy (FT-IR) spectrophotometer (Agilent Cary 360, USA), DSC (Mettler Toledo DSC 822e, Switzerland), PXRD (Philips X'Pert MPD, The Netherlands) with Cu Kα radiation, scanning electron microscope (SEM) (ZEISS EVO 18, Germany), ultraviolet (UV)-Vis spectrophotometer (Shimadzu UV-1800, Japan) for analysis at

254 nm, USP Type II dissolution apparatus (Erweka DT 600, Germany), magnetic stirrer (Remi Instruments, India), and analytical balance (Shimadzu AUW220D, Japan) with 0.1 mg sensitivity.

Co-former selection

According to the synthon-based concept, cocrystal formation largely depends on how well the functional groups of the drug and coformer interact and complement each other [6,9]. Azilsartan contains both carboxylic acid and tetrazole groups, which facilitate hydrogen bonding through their available donor and acceptor sites. These functional moieties make azilsartan a suitable candidate for cocrystal design with co-formers, such as amino acids, which possess zwitterionic centres and functional groups, including amino and carbonyl groups. In this study, various amino acids were evaluated for their potential to form supramolecular synthons with azilsartan using differential scanning calorimetry to identify unique thermal transitions indicative of successful cocrystal formation.

DSC screening results are presented in Table 1. D-alanine showed a new melting point, confirming its suitability as a co-former for the current study.

Among the screened amino acids, D-alanine was selected as the final co-former for detailed study. Although both L-tryptophan and L-proline demonstrated melting point shifts, D-alanine was chosen owing to its distinct and intense DSC endothermic peak, suggesting enhanced crystallinity and greater thermal stability of the resulting phase. Furthermore, preliminary trials revealed that the D-alanine system yielded transparent and uniform crystals with superior ease of crystallization and higher reproducibility compared to other candidates. Early solubility screening also revealed a significant increase in equilibrium solubility, indicating stronger hydrogen-bonded interactions and enhanced lattice packing efficiency. These factors collectively justified the selection of D-alanine as the optimal co-former for subsequent formulation and characterization studies.

Fabrication of drug-co-former cocrystals

Solvent evaporation

A 1:2 molar mixture of azilsartan (456.46 mg) and D-alanine (178.18 mg) was dissolved in 20 mL of an ethanol–water solvent blend (5:1 v/v) to ensure complete solubilization and uniform crystallization during evaporation. The solution, sealed with perforated foil, was stored in a desiccator under static conditions for 2–3 days to allow gradual solvent loss and crystal formation. The obtained cocrystals were separated and characterized preliminarily.

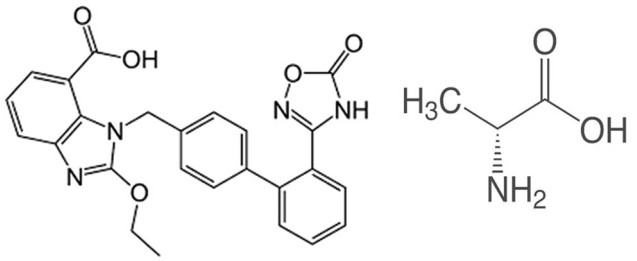

Fig. 1: Chemical structure of azilsartan and D-alanine

Table 1: Screening of Co-formers via DSC

Chemical moiety	Melting point (°C)	New melting point obtained (°C)
Azilsartan	184	-
L-arginine	212,245	220.43
L-tryptophan	253,279	187.82
L-proline	220	175.22
D-alanine	272,285	253.35

Characterization techniques

Azilsartan, D-alanine, and their cocrystals (AZL-D-Ala) were characterized using FT-IR, DSC, and PXRD. FT-IR (Agilent 360, DLATGS detector) was performed using 2–4mg samples scanned over the range of 4000–400 cm ^{1} to identify shifts in functional groups. The DSC (Mettler Toledo DSC 8221e) was used to analyze 4–5 mg samples sealed in pans, heated from 25 to 350°C at 10°C/min under nitrogen (30 mL/min). PXRD (Philips X'Pert MPD, Cu source, 30 kV, 15 mA) assessed crystallinity with scans from 5° to 65° (2θ), 0.02° step size, at 10°/min.

SEM analysis

SEM analysis of azilsartan and its cocrystals was performed using a ZEISS EVO 18 system. Samples were gold-coated under vacuum, mounted on aluminum stubs, and imaged using secondary and backscattered electron detectors at multiple magnifications.

Solubility study

Solubility was determined using the shake-flask method. Excess quantities of azilsartan and its cocrystals were added to 10 mL of distilled water and phosphate buffer (pH 7.8) and stirred continuously at 37±0.5°C using a magnetic stirrer. The samples were agitated for 24 h and monitored for equilibrium by extending the experiment to 48 h, during which no further change in concentration was observed, confirming equilibrium conditions. Samples were filtered through 0.45 μm membranes and analyzed using UV-Vis.

In vitro drug release studies

The *in vitro* release of azilsartan from the D-alanine cocrystal was studied using a USP Type II paddle apparatus (Erweka DT600). An equivalent of 40 mg of azilsartan was added to 900 mL of dissolution medium maintained at 37±0.5°C, and samples taken at regular intervals were filtered and examined at 254 nm [27].

RESULTS

Structural characterization

FT-IR spectroscopy

The FT-IR spectrum of the azilsartan–D-alanine cocrystal displayed noticeable band shifts relative to pure azilsartan, where the characteristic peaks at 1770.71 cm^{-1} (C=O stretch), 3070.78 cm^{-1} (O–H stretch), and 3319.60 cm^{-1} (N–H stretch) shifted to 1641.35 cm^{-1}, 3043.77 cm^{-1}, and 3317.67 cm^{-1}, respectively. These spectral variations reflect the formation of new hydrogen-bond interactions between the carboxylic and tetrazole groups of azilsartan and the amino or carbonyl groups of D-alanine, confirming the generation of a stable cocrystal structure (Figs. 1 and 2).

Powder X-ray diffraction studies (XRD)

PXRD analysis was conducted for pure azilsartan, D-alanine, their physical mixture, and the synthesized azilsartan–D-alanine cocrystal to confirm the formation of a new crystalline phase (Fig. 3). Pure azilsartan and D-alanine exhibited distinct and sharp diffraction peaks at characteristic 2θ values, confirming their crystalline nature. The PXRD pattern of the physical mixture represented a simple overlay of the individual diffraction peaks of both components without any noticeable shifts or disappearance, indicating the absence of solid-state interaction or phase transformation during physical blending. In contrast, the diffractogram of the azilsartan–D-alanine cocrystal displayed several new diffraction peaks along with the disappearance of certain parent peaks, suggesting the development of a unique crystalline arrangement. These changes in the diffraction profile and relative peak intensities provide compelling evidence of the formation of a novel multicomponent crystalline phase. The observed pattern distinctly differentiates the cocrystal from the physical mixture, confirming that genuine cocrystallization occurred through molecular-level interactions rather than simple mechanical mixing.

DSC

The DSC thermograms of pure azilsartan, D-alanine, their physical mixture, and the azilsartan–D-alanine cocrystal were analyzed to investigate thermal behavior and confirm cocrystal formation (Fig. 4). The thermogram of the physical mixture displayed two distinct endothermic peaks at 187.50°C and 253.45°C, corresponding to the melting points of pure azilsartan and D-alanine, respectively. The absence of any peak shifting, broadening, or merging indicates that no solid-state interaction or phase transformation occurred during simple mixing.

In contrast, the DSC thermogram of the azilsartan-D-alanine cocrystal exhibited a single, sharp endothermic peak at a new melting temperature, signifying the formation of a thermodynamically stable and homogeneous crystalline phase. This marked shift in melting behavior compared to the physical mixture provides strong thermal evidence that cocrystallization occurred only after solvent-mediated processing, rather than through mere physical blending.

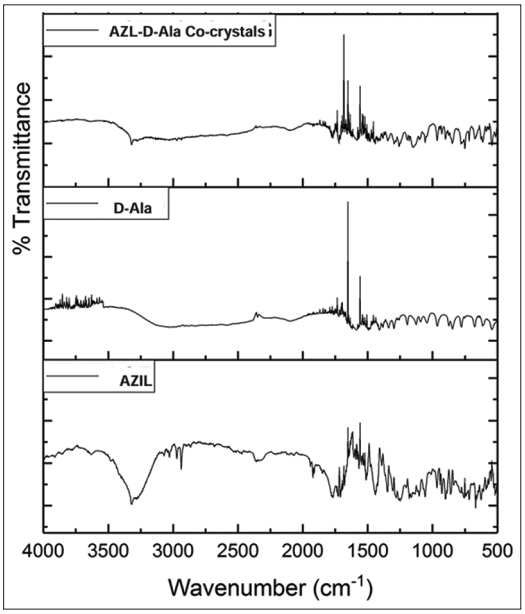

Fig. 2: Fourier transform infrared spectroscopy spectra of AZL, D-Ala, and AZL-D-Ala cocrystals

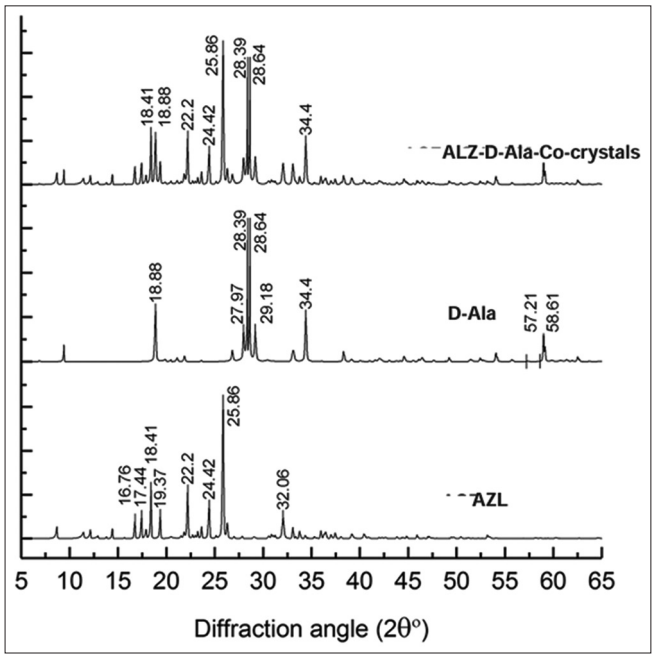

Fig. 3: PXRD of AZL, D-Ala, and AZL-D-Ala cocrystals

SEM

The surface morphology of pure azilsartan, pure D-alanine, and the azilsartan–D-alanine cocrystal was examined using scanning electron microscopy (Fig. 5). Pure azilsartan exhibited irregular plate-like particles with rough surfaces, while D-alanine appeared as fine crystalline needles. In contrast, the azilsartan–D-alanine cocrystal showed compact, block-shaped crystals with smoother surfaces and uniform morphology, indicating the formation of a new crystalline phase. These morphological changes suggest enhanced packing uniformity and reduced surface roughness, which are consistent with improved solubility and dissolution behavior. All images were captured at comparable magnifications with scale bars provided for accurate comparison.

Solubility study

Solubility studies revealed that the azilsartan–D-alanine cocrystal had higher solubility (5.53 mg/mL in water, 8.91 mg/mL in buffer) than pure azilsartan (0.048 mg/mL and 0.087 mg/mL), indicating an improvement in solubility. Although the solubility of the azilsartan–D-alanine cocrystal showed a marked enhancement, the observed solubility values for pure azilsartan (0.048 mg/mL in water and

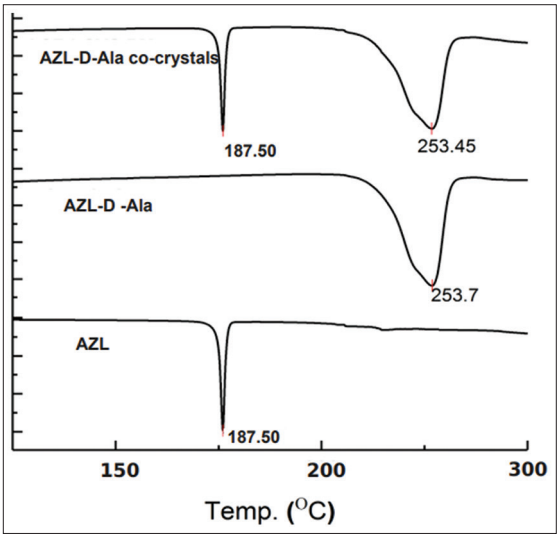

Fig. 4: DSC graph of AZL, D-Ala, and AZL-D-Ala cocrystals

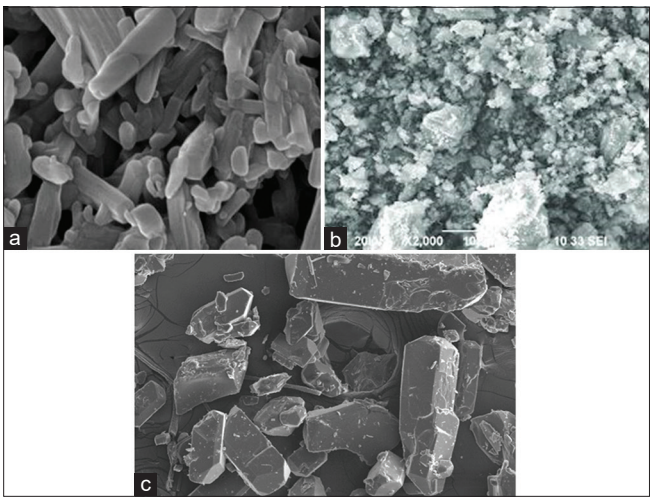

Fig. 5: Scanning electron micrographs: (a) Pure azilsartan, (b) pure D-alanine, (c) AZL-D-Ala cocrystal

0.087 mg/mL in buffer) were lower than expected for a weak acid with a pKa of 5.2 under slightly alkaline conditions. This anomaly may be explained by the presence of a highly stable crystalline polymorphic form with significant lattice energy, which restricts ionization and dissolution even in a pH 7.8 medium. Furthermore, the extended equilibration study confirmed that the solubility reached equilibrium within 24 h, as no additional increase was detected at 48 h. Thus, the low solubility can be attributed to the intrinsic structural stability of the crystalline drug rather than incomplete equilibration during the experiment.

In vitro dissolution studies

The *in vitro* dissolution profiles of pure azilsartan and the azilsartan–D-alanine cocrystal are shown in Fig. 6. The cocrystal demonstrated significantly enhanced dissolution compared with the pure drug throughout the study period. At 60 min, the cocrystal achieved 99.3±1.6% drug release, whereas pure azilsartan exhibited 73.5±2.4% release, corresponding to a 1.35-fold enhancement in dissolution efficiency. This improvement can be attributed to the modified crystal lattice, reduced crystallite size, and improved wettability of the cocrystal particles. The appearance of new crystalline faces and the disappearance of hydrophobic surface planes, as observed in SEM images, likely facilitated better medium penetration and faster drug dissolution.

DISCUSSION

The collective characterization data unequivocally confirm the successful formation of the azilsartan–D-alanine cocrystal and explain the physicochemical basis for its superior solubility and dissolution behavior. The FT-IR spectrum of the cocrystal exhibited noticeable shifts in the characteristic C=O and N–H stretching bands of azilsartan, indicating strong hydrogen-bond interactions between the carboxylic and tetrazole groups of azilsartan and the amino and carbonyl groups of D-alanine, leading to the formation of stable heterosynthons. Such supramolecular interactions weaken the intramolecular forces of the parent drug and reduce lattice energy, thereby enhancing molecular mobility and solvent accessibility. PXRD analysis further supported these findings, as the cocrystal pattern displayed new diffraction peaks and the disappearance of several parent peaks, confirming the development of a novel crystalline phase with distinct molecular packing and reduced crystallinity. The DSC thermogram revealed a single sharp endothermic peak at a new melting point lower than that of either pure azilsartan or D-alanine, signifying the formation of a homogeneous crystalline phase with diminished lattice stability, which facilitates faster dissolution. SEM micrographs showed a pronounced morphological transition from the irregular, plate-like crystals of pure azilsartan and the needle-shaped crystals of D-alanine to compact, block-shaped, and uniformly smooth cocrystal structures. This change in particle habit not only minimizes surface roughness and interparticle aggregation but also enhances wettability and solvent penetration during dissolution. The solubility study demonstrated a substantial increase in solubility for the azilsartan–D-alanine cocrystal (5.53 mg/mL in water and 8.91 mg/mL in phosphate buffer, pH 7.8) compared to pure azilsartan (0.048 mg/mL in water and 0.087 mg/mL in buffer), indicating over a 100-fold improvement. This enhancement arises from the combined effects of reduced lattice energy, improved hydrophilicity contributed by D-alanine, and the formation of a less compact crystal lattice that facilitates solvation. The *in vitro* dissolution profile (Fig. 6) corroborated these results, with the cocrystal achieving 99.3±1.6% drug release within 60 min compared to only 73.5±2.4% for the pure drug, demonstrating a 1.35-fold increase in dissolution efficiency. This pronounced improvement can be mechanistically attributed to the hydrogen-bond-mediated structural reorganization, lower crystallinity, and enhanced surface wettability of the cocrystal, which collectively enable rapid medium penetration and molecular diffusion. Therefore, the integration of spectroscopic, thermal, and morphological evidence provides a comprehensive understanding that cocrystallization with a zwitterionic amino acid like D-alanine effectively transforms azilsartan into a thermodynamically more favorable and kinetically superior crystalline form, overcoming its intrinsic solubility limitations and offering a promising strategy for improved oral bioavailability.

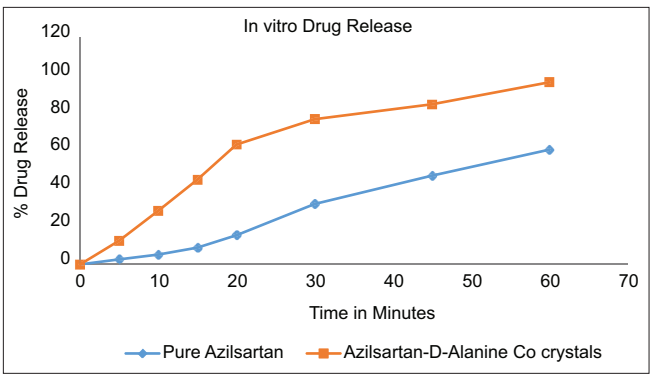

Fig. 6: *In vitro* dissolution profiles of pure azilsartan and AZL-D-Ala cocrystal in phosphate buffer (pH 7.8) at 37±0.5°C

CONCLUSION

The research successfully demonstrated the formulation of azilsartan-D-alanine cocrystals to address the solubility challenges associated with azilsartan. Utilizing a 1:2 molar ratio and the solvent evaporation technique, the cocrystals exhibited distinct physicochemical properties compared to the pure drug and coformer. FT-IR analysis indicated the formation of hydrogen bonds between azilsartan and D-alanine, while DSC thermograms revealed new melting points, confirming the creation of a new crystalline entity. PXRD patterns showed unique diffraction peaks, and SEM images displayed a transformation to a more uniform and compact morphology. These structural modifications correlated with enhanced dissolution behavior, as evidenced by *in vitro* studies where the cocrystal achieved a 1.35-fold enhancement of drug release at 60 min, compared with pure azilsartan. The improved dissolution profile suggests a potential for increased bioavailability, making the cocrystal a promising candidate for oral antihypertensive therapy. This study highlights the efficacy of amino acid-based cocrystallization in modifying and improving the physicochemical properties of poorly soluble drugs, offering a viable strategy for pharmaceutical development.

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AUTHORS CONTRIBUTIONS

All authors contributed equally to the research.

CONFLICTS OF INTEREST

The authors declare that there are no actual, potential, or perceived conflicts of interest related to this study.

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REFERENCES

1. Childs SL, Chyall LJ, Dunlap JT, Smolenskaya VN, Stahly BC, Stahly GP. Crystal engineering approach to forming cocrystals of amine hydrochlorides with organic acids. Mol Pharm. 2004;1(5):433-8.
2. Blagden N, De Matas M, Gavan PT, York P. Crystal engineering of active pharmaceutical ingredients to improve solubility and dissolution

rates. Adv Drug Deliv Rev. 2007;59(7):617-30.
3. Qiao N, Li M, Schlindwein W, Malek N, Davies A, Trappitt G. Pharmaceutical cocrystals: An overview. Int J Pharm. 2011;419(1-2): 1-11.
4. Alhalaweh A, Velaga SP. Formation of cocrystals from stoichiometric solutions of incompatible coformers: A thermodynamic perspective. Cryst Growth Des. 2010;10(8):3302-5.
5. Saraf GJ, Burade KK, Gonjari ID, Hosmani AH, Pawar AA. A review on advances in pharmaceutical co-crystal preparation routes, intellectual property perspective and regulatory aspects. Int J Curr Pharm Res. 2022 Sep 15;14:4-12.
6. Shan N, Zaworotko MJ. The role of cocrystals in pharmaceutical science. Drug Discov Today. 2008;13(9-10):440-6.
7. Zaworotko MJ. Supramolecular synthons in crystal engineering-a new organic synthesis. Chem Commun (Camb). 2001;18(1):1-9.
8. Singh A, Jaiswal V, Bisht S. Advances in cocrystals of anticancer agents: Formulation strategies and therapeutic implications. Int J Pharm Pharm Sci. 2024 Jun 1;16:27-32.
9. Yadav AV, Shete AS, Dabke AP, Kulkarni PV, Sakhare SS. Cocrystals: A novel approach to modify physicochemical properties of active pharmaceutical ingredients. Indian J Pharm Sci. 2009;71(4):359-70.
10. Wouters J, Quéré L. Pharmaceutical Salts and Cocrystals: Formation, Thermodynamics, and Product Characterization. London: Royal Society of Chemistry; 2011.
11. Nowak PM, Wietecha-Posłuszny R. The analytical eco-scale for assessing the greenness of analytical procedures. TrAC Trends Anal Chem. 2019;120:115630.
12. Almarsson Ö, Zaworotko MJ. Crystal engineering of the composition of pharmaceutical phases. Chem Commun (Camb). 2004;3(17):1889-96.
13. Bala Nagamani D, Bhaskar Reddy K, Sesha Maheswaramma K, Brito Raj S. Implementation of factorial design to optimise the formulation method of ezetimibe polymeric nanoparticle by homogenization cum ultra-sonication method. Int J Appl Pharm. 2022 Mar 7;14:151-9.
14. Kunam V, Suryadevara V, Garikapati DR, Mandava VB, Sunkara SP. Solubility and dissolution rate enhancement of ezetimibe by solid dispersion and pelletization techniques. Asian J Pharm Clin Res. 2019 Feb 15;12:407-13.
15. Shukla V, Jain P, Verma A. A review on Azilsartan medoxomil: A new angiotensin II receptor antagonist. Int J Pharm Sci Res. 2013;4(3): 874-9.
16. Patel SL, Prajapati AP, Narkhede SB. Formulation, development and evaluation of fast dissolving tablets containing azilsartan medoxomil. JETIR. 2021;8(5):571-7.
17. Srikanth K, Nagaraju T, Kumar BS. Formulation design and development of azilsartan nano-emulsion for enhanced solubility and bioavailability. Int J Drug Deliv Technol. 2023;15(1):235-40.
18. Mokale VS, Bansode AS, Bakade PS. Amelioration of bioavailability through formulating and optimizing azilsartan nanostructured lipid carriers using a heated high-pressure homogenization approach. Eur J Pharm Sci. 2022;180:106301.
19. Tanwar CS, Mehta P, Goyal R. Formulation and evaluation of solid self-microemulsifying drug delivery system for azilsartan medoxomil. Drug Dev Ind Pharm. 2020;46(3):468-76.
20. Gao L, Zhang XR. Synthesis of two novel azilsartan cocrystals: Preparation, physicochemical characterization, and solubility studies. Crystals. 2020;10(9):739.
21. Jain MK, Shaikh K, Hussain Z. Enhancing solubility and bioavailability of azilsartan medoxomil using solid dispersion technique. Pak Heart J. 2023;56(3):844-50.
22. Yaseen AA, Basha SH, Ali MR. Formulation and development of nanosuspension tablets to improve solubility and bioavailability of azilsartan. PNR J. 2022;13(1):45-50.
23. Song LY, Wang LY, Liu F, Li YT, Wu ZY, Cui WY. Simultaneously enhancing the *in vitro*/*in vivo* performances of acetazolamide using proline as a zwitterionic coformer for cocrystallization. CrystEngComm. 2019;21:3064-73.
24. Nugrahani I, Utami D, Ibrahim S, Nugraha YP, Uekusa H. Zwitterionic cocrystal of diclofenac and L-proline: Structure determination, solubility, kinetics of cocrystallization, and stability study. Eur J Pharm Sci. 2018;117:168-76.
25. Tilborg A, Norberg B, Wouters J. Pharmaceutical salts and cocrystals involving amino acids: A brief structural overview of the state-of-art. Eur J Med Chem. 2014;74:411-26.
26. Tumanova N, Tumanov N, Robeyns K, Filinchuk Y, Wouters J, Leyssens T. Structural insight into cocrystallization with zwitterionic co-formers: Cocrystals of S-naproxen. Crystengcomm. 2014;16: 8185-96.
27. Nanda A, Anand R. Formulation and evaluation of cocrystals of a bcs class II drug using glycine as coformer. Int J Appl Pharm. 2022 Nov 7;14:68-76.