

Cocrystallization of the BCS Class II Statin Rosuvastatin with Tartaric Acid by Solvent-Drop Grinding: ΔpK_a -Guided Coformer Selection, Solid-State Characterization, Enhanced In-Vitro Dissolution, and In-Vivo Antihyperlipidemic and Stability Evaluation

Vishal Patond ^{1*}, Dr. Pramod Burakle ²

¹ PhD Research Scholar, Dr. Rajendra Gode College of Pharmacy Malkapur, SGBAU Amravati, Maharashtra, India.

² PhD Research Supervisor & Principal, Dr. Rajendra Gode College of Pharmacy Malkapur, SGBAU Amravati, Maharashtra, India.

*Corresponding Author: Vishal Patond, PhD Research Scholar, Dr. Rajendra Gode College of Pharmacy Malkapur, SGBAU Amravati, Maharashtra, India. E mail: vishalpatond@gmail.com ORCID: 0000-0003-0489-8308

Abstract

Rosuvastatin is a potent HMG-CoA reductase inhibitor (statin) used to manage hypercholesterolaemia and dyslipidaemia, but as a Biopharmaceutics Classification System (BCS) class II drug it suffers from low aqueous solubility that limits its dissolution and oral bioavailability. In this work, rosuvastatin–tartaric acid cocrystals were developed to improve these properties. Tartaric acid, a generally recognized as safe (GRAS) coformer, was selected using the ΔpK_a rule, being the only screened coformer that satisfied the criterion for rosuvastatin (pK_a 4.9). Cocrystals were prepared by the solvent-drop (liquid-assisted) grinding method at drug:coformer molar ratios of 1:1, 1:2 and 2:1, and characterised by differential scanning calorimetry (DSC), Fourier-transform infrared (FT-IR) spectroscopy and powder X-ray diffraction (PXRD). DSC of the 1:1 system showed a single new endotherm at 85.01 °C, distinct from rosuvastatin (82.64 °C) and tartaric acid (126.44 °C); FT-IR confirmed drug–coformer interaction through disappearance of the tartaric-acid O–H stretch, a shift of the halogen band from 761 to 764 cm^{-1} and a carbonyl shift to 1702 cm^{-1} ; and PXRD revealed numerous new reflections confirming a distinct crystalline lattice. In 0.5 % sodium lauryl sulphate medium, the cocrystals released 99.56 % of drug within 30 min versus 68.24 % for the marketed formulation and 43.63 % for pure rosuvastatin. In the triton-X-100-induced hyperlipidaemic rat model, the cocrystals at 50 mg/kg produced the greatest improvement in the serum lipid profile (total cholesterol 93.69 ± 3.91 mg/dL versus 181.71 ± 4.08 mg/dL for control; $p < 0.01$, Dunnett's test), exceeding the standard drug at the same dose. Accelerated stability testing (40 ± 2 °C, 75 ± 5 % RH, 6 months) showed the cocrystals retained 73.62 % of content versus 61.36 % for the pure drug, both following first-order degradation kinetics. Rosuvastatin–tartaric acid (1:1) cocrystals thus provide a solid form with markedly improved dissolution, superior lipid-lowering activity and enhanced stability.

Keywords: *rosuvastatin; tartaric acid; pharmaceutical cocrystal; solvent-drop grinding; ΔpK_a rule; dissolution enhancement; triton-induced hyperlipidaemia; accelerated stability*

How to cite this article: Vishal Patond ^{1*} Dr. Pramod Burakle ². Cocrystallization of the BCS Class II Statin Rosuvastatin with Tartaric Acid by Solvent-Drop Grinding: ΔpK_a -Guided Coformer Selection, Solid-State Characterization, Enhanced In-Vitro Dissolution, and In-Vivo Antihyperlipidemic and Stability Evaluation. Int J Drug Deliv Technol. 2026;16(86s):1-7. DOI: 10.25258/ijddt.16.86s.1.

1. Introduction

The solubility of a drug in aqueous media is a key determinant of its dissolution rate and, for many orally administered compounds, of its ultimate bioavailability. A substantial proportion of marketed drugs belong to Biopharmaceutics Classification System (BCS) class II, which combines high membrane permeability with low aqueous solubility, so that dissolution becomes the rate-limiting step in absorption [1,2]. Pharmaceutical cocrystallization has gained wide acceptance as a crystal-engineering approach to improve the solubility, dissolution, stability and processability of such drugs while

retaining the covalent identity and pharmacology of the active pharmaceutical ingredient (API) [1,3].

Rosuvastatin is a potent, competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme in cholesterol biosynthesis. By suppressing hepatic cholesterol synthesis and up-regulating low-density-lipoprotein (LDL) receptors, it lowers total cholesterol, LDL, very-low-density lipoprotein (VLDL) and triglycerides while raising high-density lipoprotein (HDL), and is widely used in the management of hypercholesterolaemia and dyslipidaemia [4]. As a BCS class II statin, however,

its clinical utility is constrained by poor aqueous solubility, which slows dissolution and contributes to modest and variable oral bioavailability. Enhancing its dissolution behaviour through cocrystallization is therefore an attractive formulation objective [4,5].

Rational coformer selection underpins any cocrystallization campaign. The ΔpK_a rule, based on the difference between the pK_a values of the acidic and basic partners, offers a convenient predictive filter, with values between 0 and 1 favouring neutral cocrystal rather than salt formation [6]. Preparation methods range from solution crystallization to mechanochemical routes; solvent-drop (liquid-assisted) grinding, in which a catalytic amount of solvent accelerates molecular reorganisation during grinding, is a simple, green and scalable technique that has been used successfully for statin cocrystals [5]. Confirmation of cocrystal formation relies on a convergent set of solid-state techniques—DSC for new melting behaviour, FT-IR for the specific hydrogen-bonding interaction, and PXRD for the emergence of a new crystalline lattice [7].

The present study describes the design, preparation and comprehensive evaluation of rosuvastatin–tartaric acid cocrystals. Tartaric acid, a GRAS dicarboxylic-acid coformer, was selected by the ΔpK_a rule and the cocrystals were prepared by solvent-drop grinding at three stoichiometric ratios. Solid-state characterization was performed by DSC, FT-IR and PXRD; the biopharmaceutical benefit was assessed by comparative in-vitro dissolution against pure drug and a marketed formulation; the pharmacological performance was evaluated in the triton-X-100-induced hyperlipidaemic rat model; and the robustness of the new form was established by accelerated stability testing under ICH conditions.

2. Materials and Methods

2.1. Materials

Rosuvastatin was used as the model BCS class II statin and tartaric acid as the GRAS coformer. Ethanol served as the grinding liquid and sodium lauryl sulphate (SLS) as the dissolution surfactant. Triton X-100 (Sigma-Aldrich Chemicals Ltd., Hyderabad, India) was used to induce experimental hyperlipidaemia. All other reagents were of analytical grade and used as received. A commercially available rosuvastatin formulation was used as the reference product for dissolution comparison.

2.2. Coformer selection (ΔpK_a rule)

The likelihood of cocrystal formation was predicted using the ΔpK_a value method. Among the coformers screened, only tartaric acid satisfied the criterion for rosuvastatin (pK_a 4.9), yielding a ΔpK_a within the favourable range for cocrystal formation, and was therefore selected for further work.

2.3. Preparation of cocrystals (solvent-drop grinding)

Cocrystals were prepared by the solvent-drop (liquid-assisted) grinding method. Rosuvastatin and tartaric acid were combined at molar ratios of 1:1 (360 mg : 122 mg), 1:2 (360 mg : 244 mg) and 2:1 (720 mg : 122 mg) and ground manually in a mortar and pestle with the dropwise addition of ethanol (5 mL). The ground mass was dried to remove solvent and passed through a number-60 sieve. A physical mixture was prepared in parallel by simply blending equal proportions of the two components without any solvent.

2.4. Solid-state characterization

DSC was performed on a DSC Q10 (V9.9, Build 303) instrument. As the melting points of rosuvastatin (82 °C) and tartaric acid (122 °C) lie below 160 °C, the heating programme was set between 20 °C and 160 °C. FT-IR spectra of rosuvastatin, tartaric acid, their physical mixture and the cocrystals were recorded on an FT-IR Alpha Bruker (1206 0280) spectrometer using the KBr disc technique. Powder X-ray diffraction patterns were obtained on an X'Pert PRO diffractometer by continuous scanning of the 2θ angle, and characteristic peak positions with relative intensities were recorded for all four samples.

2.5. In-vitro dissolution study

Dissolution studies were carried out on a Lab India DS-8000 USP Type II (paddle) apparatus. Forty milligrams of pure rosuvastatin, the equivalent of the cocrystals and the marketed formulation were tested in 0.5 % SLS solution as the dissolution medium, at a paddle speed of 50 rpm and 37 ± 0.5 °C over 30 min. Samples (5 mL) were withdrawn at intervals, filtered through a 0.45 μ m syringe filter and assayed; the percent cumulative drug release was calculated and fitted to zero-order and first-order kinetic models.

2.6. In-vivo antihyperlipidaemic study

The lipid-lowering activity was evaluated in the triton-X-100-induced hyperlipidaemic rat model. Animals were assigned to four groups: group I (control) received intragastric normal saline; group II received rosuvastatin–tartaric acid cocrystals at 25 mg/kg (half the standard dose); group III received cocrystals at 50 mg/kg (equivalent dose); and group IV received standard rosuvastatin at 50 mg/kg. Serum total cholesterol (TC), triglycerides (TG), HDL, LDL and VLDL were determined, and the data were analysed by one-way ANOVA with Dunnett's multiple comparisons test against the triton-X-100 control.

2.7. Accelerated stability study

Accelerated stability testing was conducted in accordance with ICH guidance. Pure drug and cocrystals were stored at 40 ± 2 °C and 75 ± 5 %

Cocrystallization of the BCS Class II Statin Rosuvastatin with Tartaric Acid by Solvent-Drop Grinding: ApKa-Guided Coformer Selection, Solid-State Characterization, Enhanced In-Vitro Dissolution, and In-Vivo Antihyperlipidemic and Stability Evaluation

relative humidity for 6 months; samples were withdrawn at 0, 3 and 6 months and analysed in triplicate by HPLC. The area under the curve (AUC) was used to quantify drug content, and degradation kinetics were modelled.

3. Results and Discussion

3.1. Differential scanning calorimetry

Pure rosuvastatin displayed a distinct melting endotherm at 82.64 °C (99.41 % purity) and tartaric acid at 126.44 °C, each free of extraneous peaks. In the physical mixture the two component endotherms were replaced by a single sharp peak at 85.60 °C, an early sign of a physicochemical interaction on heating. The cocrystals produced a well-defined single endotherm at 85.01 °C with no additional peaks, confirming cocrystallization. Across the stoichiometric series, only the 1:1 ratio yielded a clean single new endotherm, whereas the 1:2 and 2:1 ratios showed the cocrystal peak accompanied by residual component peaks, indicating incomplete conversion; the 1:1 ratio was therefore selected as optimal (Table 1).

Table 1. DSC data for rosuvastatin, tartaric acid, their physical mixture and cocrystals.

System / ratio	Observed DSC endotherm (°C)	Interpretation
Rosuvastatin (pure)	82.64 (99.41% purity)	Crystalline drug
Tartaric acid (pure)	126.44	Crystalline coformer
Physical mixture	85.60 (single peak)	Physicochemical interaction
Cocrystal 1:1	85.01 (single new peak)	Successful cocrystal (optimal)
Cocrystal 1:2	Cocrystal peak + component peaks	Incomplete conversion
Cocrystal 2:1	Cocrystal peak + component peaks	Incomplete conversion

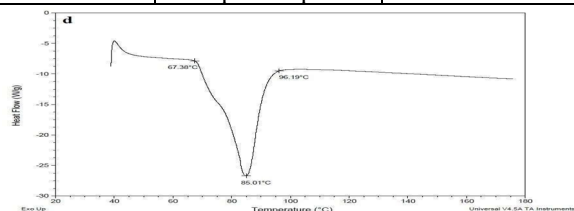


Figure 1: DSC thermogram of Rosuvastatin and tartaric acid (1:1)

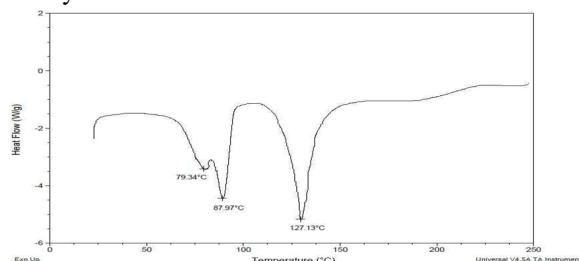


Figure 2: DSC thermogram of Rosuvastatin and tartaric acid (1:2)

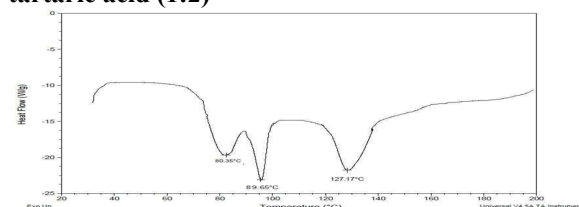


Figure 3: DSC thermogram of Rosuvastatin and tartaric acid (2:1)

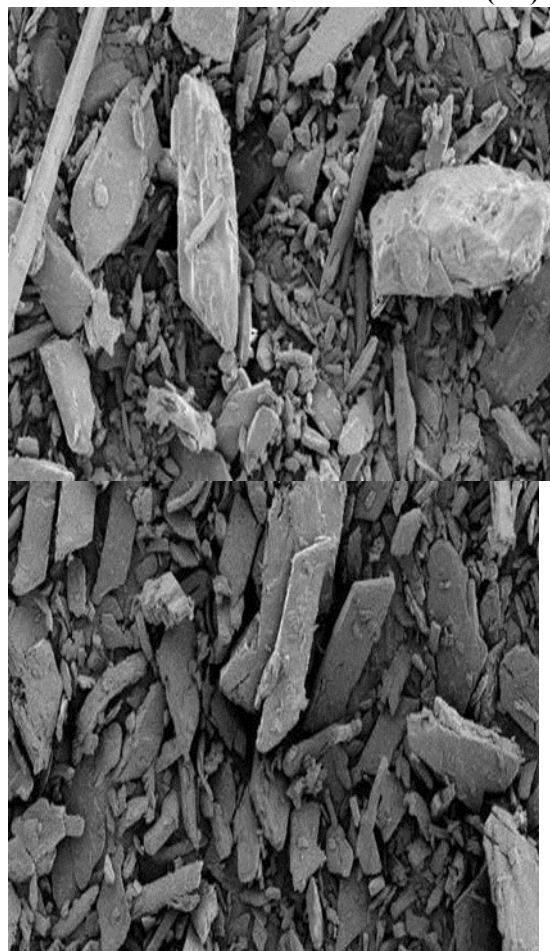


Figure 4: Microscopic view of Rosuvastatin: tartaric acid (1:1) cocrystals which exhibits crystalline nature of co-crystals (100X)

3.2. FT-IR spectroscopy

The FT-IR spectrum of rosuvastatin showed its characteristic C–H (aromatic) stretch and a halogen

Cocrystallization of the BCS Class II Statin Rosuvastatin with Tartaric Acid by Solvent-Drop Grinding: ApKa-Guided Coformer Selection, Solid-State Characterization, Enhanced In-Vitro Dissolution, and In-Vivo Antihyperlipidemic and Stability Evaluation

(C–Cl) band at 761 cm^{-1} , while tartaric acid presented its acidic carboxylic C–O stretch and a free O–H band in the $3609\text{--}3794\text{ cm}^{-1}$ region. In the physical mixture these bands were largely preserved, with only minor shifts consistent with weak van der Waals forces, indicating that solvent-free blending produced no true chemical interaction. In the cocrystals, by contrast, clear evidence of drug–coformer interaction was observed: the free O–H stretch of tartaric acid disappeared, the halogen band shifted from 761 to 764 cm^{-1} , and the carbonyl (C=O) stretches of tartaric acid (1684 cm^{-1}) and rosuvastatin (1648 cm^{-1}) shifted to 1702 cm^{-1} . Together with the loss of the C–O stretch at 2992 cm^{-1} seen in the physical mixture, these changes confirm hydrogen bonding between the drug and the coformer (Table 2).

Table 2. Key FT-IR changes confirming rosuvastatin–tartaric acid interaction.

Band / functional group	Rosuvastatin / tartaric acid	Change in cocrystal
Free O–H stretch (tartaric acid)	$3609\text{--}3794\text{ cm}^{-1}$	Absent
Halogen (C–Cl) band	761 cm^{-1}	Shift to 764 cm^{-1}
C=O carbonyl stretch	$1648 / 1684\text{ cm}^{-1}$	Shift to 1702 cm^{-1}
C–O stretch	2992 cm^{-1} (physical mixture)	Absent in cocrystal

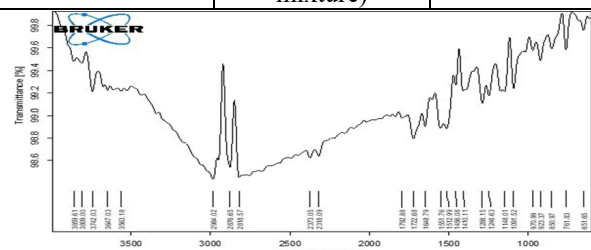


Figure 5: FT-IR spectrum of Rosuvastatin

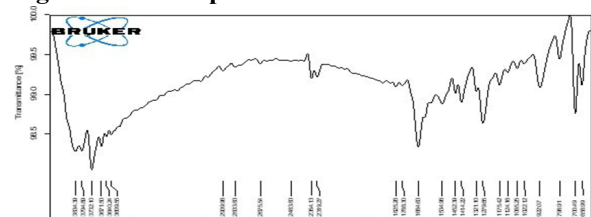


Figure 6: FT-IR spectrum of tartaric acid

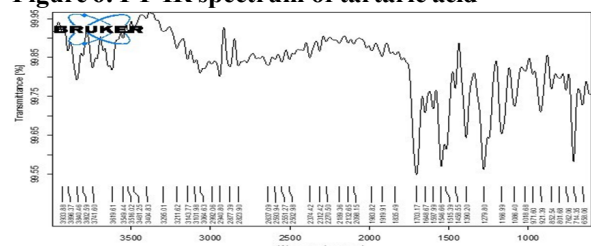


Figure 7: FT-IR spectrum of physical mixture

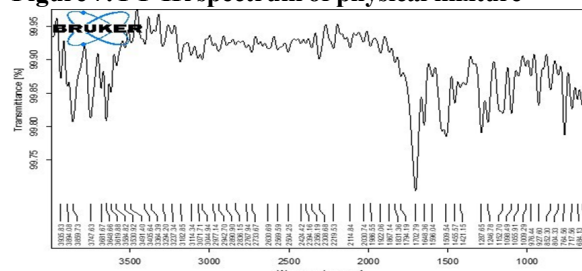


Figure 8: FT-IR spectrum of cocrystals

3.3. Powder X-ray diffraction

PXRD confirmed the formation of a new crystalline phase. Rosuvastatin exhibited characteristic 2θ reflections at 11.80° , 12.46° , 15.06° , 21.83° , 25.85° and 27.45° , and tartaric acid its own sharp reflections. The physical mixture reproduced the parent reflections (principal peak near 8.55°), confirming preservation of the individual lattices on blending. The cocrystals, however, displayed a markedly different pattern with numerous new reflections at 2θ values of 6.27° , 8.11° , 11.26° , 11.85° , 14.33° , 15.68° , 16.60° , 20.80° , 22.15° , 30.58° , 38.77° and 43.55° , while the characteristic peaks of both parent solids were absent. The emergence of these new peaks, distinct from those of the physical mixture, is diagnostic of a novel crystal structure formed through drug–coformer hydrogen bonding, corroborating the DSC and FT-IR results.

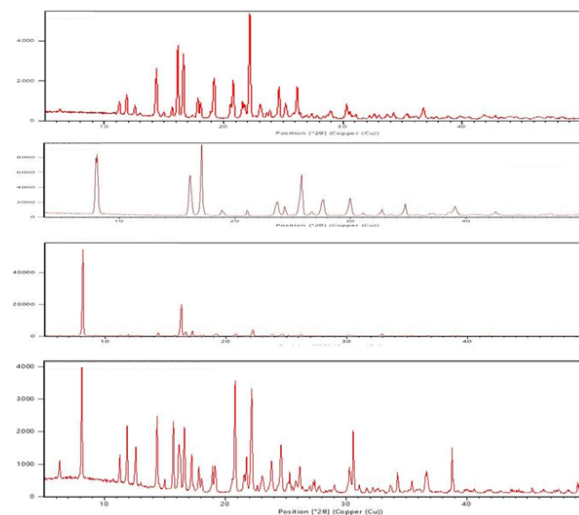


Figure 9: XRD spectrum of Rosuvastatin, tartaric acid, their physical mixture and cocrystals

3.4. In-vitro dissolution

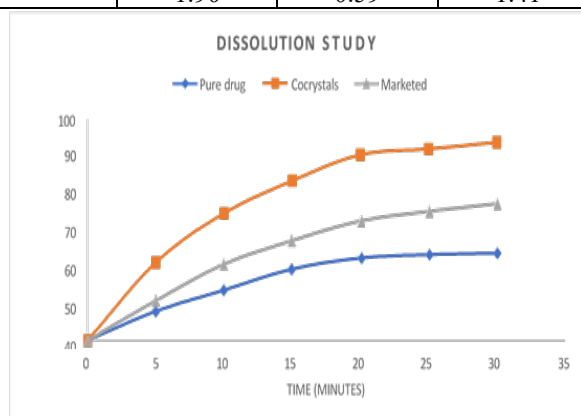
The dissolution study in 0.5 % SLS medium demonstrated a pronounced enhancement of drug release for the cocrystals. Pure rosuvastatin released only 43.63 % of drug over 30 min, reflecting its poor aqueous solubility, whereas the marketed formulation reached 68.24 % and the cocrystals achieved 99.56 % over the same interval (Table 3). The cocrystals

Cocrystallization of the BCS Class II Statin Rosuvastatin with Tartaric Acid by Solvent-Drop Grinding: ApKa-Guided Coformer Selection, Solid-State Characterization, Enhanced In-Vitro Dissolution, and In-Vivo Antihyperlipidemic and Stability Evaluation

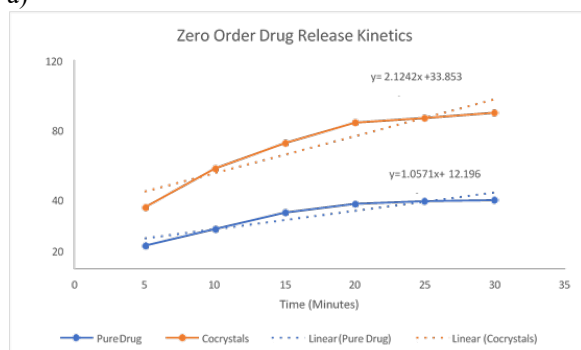
outperformed both comparators at every time point. Kinetic modelling showed that both the pure drug and the cocrystals followed first-order release, with the cocrystals giving the best first-order fit ($R^2 = 0.9606$), indicating concentration-dependent release (Table 4).

Table 3. Percent cumulative drug release (mean $\pm$ S.D.) in 0.5 % SLS medium.

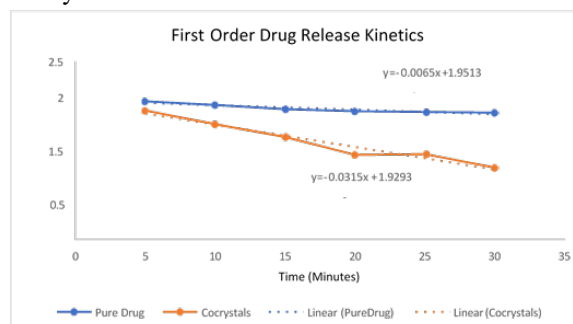
Time (min)	Pure drug (%)	Cocrystal (%)	Marketed (%)
5	14.56 $\pm$ 2.38	38.97 $\pm$ 1.98	19.79 $\pm$ 0.95
10	25.17 $\pm$ 1.99	63.56 $\pm$ 2.11	37.95 $\pm$ 1.42
15	35.63 $\pm$ 1.81	79.78 $\pm$ 2.33	49.84 $\pm$ 3.11
20	41.17 $\pm$ 2.36	92.80 $\pm$ 1.89	59.64 $\pm$ 2.88
25	42.87 $\pm$ 2.89	95.71 $\pm$ 3.34	64.42 $\pm$ 1.93
30	43.63 $\pm$ 1.90	99.56 $\pm$ 0.59	68.24 $\pm$ 1.41



a)



b)



c)

Figure 4.60 (A) Comparison of drug release study (B) Zero order kinetics (C) First order kinetics

Table 4. In-vitro release kinetic modelling of rosuvastatin and its cocrystals.

Model	Pure drug	Cocrystal
Zero-order (equation)	$y = 1.0571x + 12.196$	$y = 2.1242x + 33.853$
Zero-order R^2	0.8725	0.8854
First-order (equation)	$y = -0.0065x + 1.9513$	$y = -0.0315x + 1.9293$
First-order R^2	0.8993	0.9606

3.5. In-vivo antihyperlipidaemic activity

In the triton-X-100-induced hyperlipidaemic model, the control group showed the expected elevation of serum lipids, whereas all drug-treated groups produced significant improvements in the lipid profile ($p < 0.01$, Dunnett's test). The full-dose cocrystals (group III, 50 mg/kg) produced the greatest effect, reducing total cholesterol to 93.69 ± 3.91 mg/dL and triglycerides to 85.44 ± 3.52 mg/dL (versus 181.71 ± 4.08 and 178.95 ± 4.69 mg/dL, respectively, in the control) and simultaneously raising HDL to 39.98 ± 1.19 mg/dL. Notably, at the same dose the cocrystals outperformed the standard rosuvastatin (group IV) on total cholesterol, triglycerides and LDL, and even the half-dose cocrystals (group II, 25 mg/kg) produced measurable lipid lowering. This enhanced pharmacodynamic response is attributable to the improved dissolution and consequent absorption of the cocrystal form (Table 5).

Table 5. Serum lipid profile (mg/dL; mean $\pm$ S.D.) in the triton-induced model. ** $p < 0.01$ versus control (Dunnett's test); ns = not significant. TC, total cholesterol; TG, triglycerides; HDL/LDL/VLDL, lipoprotein fractions.

Group (dose)	TC	TG	HDL	LDL	VLDL
I – Control	181.7 $\pm$ 4.08	178.9 $\pm$ 4.69	30.95 $\pm$ 4.76	114.8 $\pm$ 3.03	30.30 $\pm$ 3.67

Cocrystallization of the BCS Class II Statin Rosuvastatin with Tartaric Acid by Solvent-Drop Grinding: ApKa-Guided Coformer Selection, Solid-State Characterization, Enhanced In-Vitro Dissolution, and In-Vivo Antihyperlipidemic and Stability Evaluation

II – Cocrystal 25 mg/kg	167.6 5 ± 5.09* *	128.4 2 ± 4.01* *	29.19 ± 0.62 ns	107.2 1 ± 2.43* *	28.07 ± 1.48 ns
III – Cocrystal 50 mg/kg	93.69 ± 3.91* *	85.44 ± 3.52* *	39.98 ± 1.19* *	48.27 ± 2.19* *	16.62 ± 1.03* *
IV – Rosuvastat in 50 mg/kg	113.6 1 ± 2.68* *	103.4 7 ± 2.13* *	34.87 ± 2.08 ns	61.23 ± 3.80* *	21.80 ± 2.51* *

3.6. Accelerated stability

Under accelerated conditions ($40 \pm 2^\circ\text{C}$, $75 \pm 5\%$ RH), the cocrystals retained substantially more of their initial content than the pure drug over 6 months. The percent drug remaining fell from $98.75 \pm 0.121\%$ to $73.62 \pm 0.691\%$ for the cocrystals, compared with a decline from $99.53 \pm 0.151\%$ to $61.36 \pm 0.531\%$ for the pure drug. Consistent HPLC AUC analysis showed the rosuvastatin AUC decreasing from 125927 (0 months) to 105291 (3 months) and 78292 (6 months). Both samples followed first-order degradation kinetics, but the markedly higher retention of the cocrystals demonstrates that cocrystallization with tartaric acid also improves the physicochemical stability of rosuvastatin (Table 6).

Table 6. Percent drug remaining under accelerated stability conditions (HPLC).

Time (months)	Cocrystal (% remaining)	Pure drug (% remaining)
0	98.75 ± 0.121	99.53 ± 0.151
3	93.05 ± 4.62	83.46 ± 1.129
6	73.62 ± 0.691	61.36 ± 0.531

4. Conclusion

Rosuvastatin–tartaric acid cocrystals were rationally designed using the ΔpKa rule and successfully prepared by the simple, green solvent-drop grinding technique, with the 1:1 drug:coformer ratio identified as optimal. A convergent body of solid-state evidence—a single new DSC endotherm at 85.01°C , characteristic FT-IR changes (loss of the tartaric-acid O–H stretch, halogen shift $761 \rightarrow 764\text{ cm}^{-1}$ and carbonyl shift to 1702 cm^{-1}), and numerous new PXRD reflections—confirmed the formation of a distinct cocrystalline phase. The cocrystals delivered a substantially enhanced in-vitro dissolution profile (99.56% at 30 min) relative to the marketed formulation (68.24%) and pure drug (43.63%), which translated into superior in-vivo lipid-lowering activity in the triton-induced hyperlipidaemic model—exceeding the standard drug at an equivalent dose and showing a dose-sparing benefit—and into

improved physicochemical stability (73.62% versus 61.36% content retention over 6 months). Collectively, these findings establish rosuvastatin–tartaric acid (1:1) cocrystals as a promising solid form for improving the biopharmaceutical and therapeutic performance of this poorly soluble statin, and reinforce cocrystallization as an effective strategy for BCS class II drugs.

Author Contributions

[First Author]: investigation, methodology, formal analysis, writing—original draft. XYZ: pharmacological evaluation, validation, writing—review and editing. ABC: conceptualization, supervision, resources, writing—review and editing. All authors read and approved the final manuscript.

Ethics Statement

The in-vivo antihyperlipidaemic study was conducted in accordance with institutional and national guidelines for the care and use of laboratory animals, following approval by the Institutional Animal Ethics Committee (IAEC). [Insert IAEC approval/protocol number.]

Conflict of Interest

The authors declare no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

References

- [1] Rao RP, Natarajan J, Khanra S, Pachiyappan JK, Nizam I, Muralidhara A, Selvaraj J, Selvamuthukumar S. Advances in pharmaceutical cocrystals and nano-cocrystals: strategies for enhancing solubility and translating to clinical use. *AAPS PharmSciTech*. 2025;26(8):233. doi:10.1208/s12249-025-03228-y
- [2] Babu NR, Nagpal D, Ankola D, Awasthi R. Evolution of solid dispersion technology: solubility enhancement using hydroxypropyl methylcellulose acetate succinate: myth or reality? *Assay Drug Dev Technol*. 2022;20(4):149–163. doi:10.1089/adt.2022.016
- [3] Mannava MKC, Garai A, Nangia AK. Diffusion and flux improvement of drugs through complexation. *Mol Pharm*. 2023;20(5):2293–2316. doi:10.1021/acs.molpharmaceut.3c00159
- [4] Vemuri VD, Lankalapalli S. Cocrystal construction between rosuvastatin calcium and L-asparagine with enhanced solubility and dissolution rate. *Turk J Pharm Sci*.

2021;18(6):790–798.

doi:10.4274/tjps.galenos.2021.62333

- [5] Khan FM, Ahmad M, Idrees HA. Simvastatin–nicotinamide co-crystals: formation, pharmaceutical characterization and in vivo profile. *Drug Des Devel Ther.* 2020;14:4303–4313. doi:10.2147/DDDT.S270742
- [6] 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;74:411–426. doi:10.1016/j.ejmech.2013.11.045
- [7] Garbacz P, Wesolowski M. Benzodiazepines co-crystals screening using FTIR and Raman spectroscopy supported by differential scanning calorimetry. *Spectrochim Acta A Mol Biomol Spectrosc.* 2020;234:118242. doi:10.1016/j.saa.2020.118242
- [8] Sharapova A, Ol'khovich M, Blokhina S. Carvedilol pharmaceutical cocrystals: preparation, advanced characterization and dissolution behavior. *AAPS PharmSciTech.* 2026;27(2):79. doi:10.1208/s12249-025-03317-y
- [9] Alam Q, Ganeshpurkar A, Singh SK, Krishnamurthy S. Preparation, characterization, in-vitro and in-vivo pharmacokinetic evaluation of thermostable dimethyl fumarate cocrystals. *J Pharm Sci.* 2023;113(3):647–658. doi:10.1016/j.xphs.2023.07.001
- [10] Ouiyangkul P, Tantishaiyakul V, Hirun N. Exploring potential cofomers for oxyresveratrol using principal component analysis. *Int J Pharm.* 2020;587:119630. doi:10.1016/j.ijpharm.2020.119630