RESEARCH PAPER

Triamterene: Synthetic Strategies, Complex Formation, and Biological Activities—A Mini-Review

Anjali[1], Shraddha Upadhyay[2*]

[1,2]Department of Chemistry, Swami Vivekanand Subharti University, Meerut, Uttar Pradesh, India - 250005.

Corresponding Author: Shraddha Upadhyay, Department of Chemistry, Swami Vivekanand Subharti University, Meerut, Uttar Pradesh, India
Email: dr.shrupa@gmail.com

Received: 22 September 2026; Accepted: 14 October 2026 ; Available Online: 07 November 2026

ABSTRACT

Triamterene is a potassium-sparing diuretic that has a pteridine scaffold that allows for a variety of chemical modifications and intermolecular interactions. The synthetic approaches, physicochemical properties, complex formation and biological activities of this compound are discussed in this narrative mini-review. The condensation of an aminonitrosopyrimidine precursor with phenylacetonitrile has been established, and related studies have been carried out on positional and heterocyclic isomers. Salt formation, solid dispersions and macrocyclic inclusion systems have been used to improve solubility or dissolution under experimental conditions. Charge-transfer complexes have additional applications in pharmaceutical analysis. In addition to its well-established inhibition of epithelial sodium channels, preclinical studies have identified antifolate-associated activity in mismatch-repair-deficient tumour models, histone deacetylase inhibition with cisplatin sensitisation, and chloride intracellular channel 1 inhibition in glioblastoma models. These results warrant further investigation, but are not proof of clinical anticancer activity. Hyperkalaemia and crystalline nephropathy are still important safety issues. Future work should include structural characterization, formulation stability, pharmacokinetics, and exposure–response assessment to evaluate if enhanced pharmaceutical properties and experimental biological activities lead to clinical benefit.

Keywords: Triamterene; Pteridines; Complex formation; Solubility enhancement; Drug repurposing.
How to cite this article: Anjali, Upadhyay S., Triamterene: Synthetic Strategies, Complex Formation, and Biological Activities – A Mini-Review. Int J Drug Deliv Technol. 2026;16(90s): 78-84; DOI: 10.25258/ijddt.16.90s.8
Source of Support: Nil.
Conflict of interest: None

1 INTRODUCTION

Triamterene is a potassium-sparing diuretic that has been shown to have a pharmacological effect of inhibiting epithelial sodium channels in the distal nephron. It decreases the reabsorption of sodium, which means that the electrical driving force for potassium secretion is also decreased, giving a mechanistic explanation for its potassium-conserving effects [1]. It is also a chemically interesting compound, being 2,4,7-triamino-6-phenylpteridine. The nitrogen-rich heterocyclic framework and exocyclic amino groups enable significant intermolecular hydrogen bonding, which connects the molecular structure to the organisation in the solid state [2].

The therapeutic use of triamterene is well known, but the drug has also been used to exploit intermolecular association for controlling its pharmaceutical properties. The poor aqueous solubility has spurred research into other solid forms and inclusion systems. Molecular salts with better solubility and dissolution properties have been obtained by crystallisation with appropriate acidic coformers [3]. Cyclodextrin inclusion systems have also been shown to be effective in enhancing drug release and diuretic activity in rats [4]. The results show the need to differentiate between salt formation, host–guest inclusion and other types of complexation in assessing their pharmaceutical significance.

Triamterene is also gaining interest in biological activities other than diuresis. Selective activity against DNA mismatch-repair-deficient tumour cells, via an antifolate-associated mechanism, and histone deacetylase inhibition associated with sensitisation of resistant models of lung cancer to cisplatin have been

reported in preclinical studies [5,6]. These observations can be used as a foundation for drug-repurposing studies, but it is important to distinguish between experimental activity and proven clinical efficacy.

This mini-review summarizes the synthetic chemistry, physicochemical behaviour, complex systems and biological activities of triamterene. It explores the impact of structural features on pharmaceutical performance and elucidates the evidence required to correlate chemical modification or formulation development with therapeutic benefit.

2 LITERATURE SEARCH AND SELECTION

The present narrative mini-review is based on targeted searches of PubMed and publisher-hosted literature using combinations of the search term “triamterene” with “synthesis,” “physicochemical properties,” “crystal structure,” “salt formation,” “inclusion complexes,” “charge-transfer complexes,” “pharmacokinetics,” and “biological activity.” The publications were chosen based on their relevance to synthetic methods, structural characterization, pharmaceutical applications and biological effects. Primary research articles were given preference. Literature pertaining to triamterene, its structural analogues and its complex systems was treated separately to avoid confusing the attribution of reported properties and activities.

3 CHEMICAL STRUCTURE AND PHYSICOCHEMICAL PROPERTIES

Triamterene has a pteridine nucleus (pyrimidine and pyrazine rings fused together), containing amino groups at positions 2, 4, and 7, and a phenyl group at position 6. This is a multiple hydrogen-bond donor/acceptor arrangement. The crystallographic and graph-set analysis has shown that in the parent solid there is an extended network of hydrogen bonds whose arrangement has an effect on the molecular packing [2]. The scaffold thus allows for self-association and interactions with complementary coformers, but the solid form is dependent on the chemical environment and crystallisation conditions.

The protonation of triamterene is of special interest for its physicochemical and pharmacological behaviour. Triamterene is a weak base, with a reported pKa of ~6.2. Electrophysiological experiments indicated that the inhibition of the epithelial sodium channel was greater at lower extracellular pH, which is in accordance with greater potency of the protonated species [1]. Protonation also allows for the formation of salts with appropriate acids. Protonation at the N1 position has been identified in the investigated triamterene salts with the help of confocal Raman microspectroscopy, complemented by structural and physicochemical evaluation [7]. Therefore, acid–base behaviour influences intermolecular organisation and interaction with the pharmacological target.

The poor aqueous solubility of the parent compound has promoted screening in the solid form. Molecular salts prepared by cocrystallisation techniques have been found to show improved solubility and dissolution compared with triamterene [3]. These improvements must be considered in terms of the counterion, the dissolution medium, and the stability of the solid form prepared.

Solvation is another complicating factor. Dahl et al. described crystals with N,N-dimethylformamide and water in the lattice, and showed that differences in melting behaviour do not necessarily establish polymorphism [8]. It is thus important to differentiate between anhydrous forms, solvates and hydrates when comparing thermal properties and pharmaceutical performance. These forms and their behaviour during preparation and storage can be assessed using complementary diffraction, spectroscopy and thermal analysis.

4 SYNTHETIC STRATEGIES AND STRUCTURAL MODIFICATION

The classical synthesis of triamterene involves the formation of the pteridine ring from a suitably substituted pyrimidine precursor. The routes to 7-amino- and 7-hydroxypteridines developed by Spickett and Timmis [9] provided the foundation for the work described here. In the route relevant to triamterene, the second heterocyclic ring is formed by reacting 2,4,6-triamino-5-nitrosopyrimidine with phenylacetonitrile. The resulting product will have the amino substituents at positions 2 and 4, and the phenyl group at position 6 and the amino group at position 7. The method directly correlates the selection of the precursors with the substitution pattern of the final pteridine.

The route provides a good separation between the heterocyclic framework and the modification of the final product. Subsequent functionalisation can be performed on a pre-existing scaffold, while the change of the precursor or coupling component can change the substitution pattern introduced during the ring formation. This distinction is useful for medicinal chemistry as it may alter the spatial arrangement of the hydrogen-bonding sites and the electronic properties of the heterocycle. These changes must be confirmed by structure rather than elemental composition.

Historical studies also explored this structural space through the synthesis of pteridine isomers of triamterene. Weinstock and Dunoff studied positional isomers in the pteridine series [10]. Graboyes and coworkers expanded the comparison to pyrimidopyrimidine isomers, which are isomers of a related fused heterocyclic framework [11]. The properties of these compounds should be attributed to

the individual compounds and not inferred as properties of triamterene; they are examples of scaffold and substitution-pattern variation.

Comparisons of further synthetic development would be improved by reporting isolated yield, impurity profiles, reproducibility, solvent requirements, and scalability under consistent conditions. In the case of biologically directed analogue synthesis, novelty should be linked to the observed changes in target activity, selectivity and pharmaceutical properties. This would assist in differentiating changes that would aid in chemical preparation from changes that would make the compound more useful.

5 COMPLEX FORMATION AND PHARMACEUTICAL APPLICATIONS

5.1 Salt Formation, Solvates, and Crystal Engineering

Triamterene has multiple amino groups and basic ring nitrogen atoms, allowing it to engage in several modes of intermolecular association. Dittert and co-workers conducted early phase-solubility studies that showed the presence of protonated and unprotonated triamterene in acidic systems as complex salts [12]. This work demonstrated that changes in solubility as a function of acidity could reflect equilibria that involve more than a simple one-to-one salt.

Later crystallographic investigations have shed light on the diversity of the structures of triamterene solids. Rehman et al. prepared crystalline forms with carboxylic acids, which are generally recognised as safe coformers, and active pharmaceutical ingredients, such as ibuprofen, by using liquid-assisted grinding and solvent evaporation methods [13]. The salts and solvates that were obtained showed different hydrogen-bonding motifs, such as tape and sheet motifs. Protonation, counterion identity and solvent incorporation in these structures show how the parent hydrogen-bond network can be reorganised.

Solid dispersions are an alternative solution. Onoda and coworkers prepared triamterene systems with ascorbic acid or ascorbic acid 2-glucoside by solvent evaporation [14]. Reduced crystallinity and intermolecular interactions were supported by diffraction, thermal and spectroscopic results. In the reported dissolution experiment, approximately 90% of triamterene dissolved within 3 min from the 1:1 systems, whereas approximately 30% dissolved from the drug alone. These results indicate enhanced dissolution under the experimental conditions, but do not provide quantitative estimates of systemic bioavailability.

5.2 Cyclodextrin and Other Host–Guest Inclusion Systems

Macrocyclic hosts provide another way to alter the apparent solubility of triamterene. In β-cyclodextrin systems, inclusion of the phenyl group within the host cavity has been linked to enhanced dissolution. The coevaporated system investigated by Mukne and Nagarsenker also resulted in greater sodium excretion after oral administration in rats than did triamterene powder [4]. This is a pharmacodynamic observation and not a direct measurement of plasma exposure.

Maeda et al. studied sulfobutylether-β-cyclodextrin and found the association constant to be 510 L/mol [15]. Insertion of the triamterene phenyl ring from the secondary hydroxyl face of the host was supported by NMR experiments. Of the preparation methods tested, mechanochemical treatment resulted in a system that had better dissolution and did not require organic solvents. Results support further formulation development, but improved oral bioavailability was still a proposed outcome that needs to be confirmed via pharmacokinetic studies.

Cyclodextrins are not the only compounds that can form inclusion systems. Chao et al. studied the association between triamterene and p-sulfonatocalix[6]arene by a combination of spectroscopic, microscopic, and thermal techniques [16]. A 1:1 complex was found at pH 6.5, which was more soluble in water than the uncomplexed drug. The results expand the host structure options available for the study of triamterene delivery, while formulation stability and biological compatibility remain development considerations.

5.3 Charge-Transfer Complexes and Analytical Applications

Triamterene is also an electron donor to appropriate organic acceptors. Aldawsari et al. studied its charge-transfer complexes with 7,7,8,8-tetracyanoquinodimethane and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone by spectroscopic measurements and computational calculations [17]. The coloured complexes were used for spectrophotometric assays of triamterene in pure and pharmaceutical preparations. Their principal demonstrated application was analytical quantification.

These are not synonymous with metal coordination or therapeutic enhancement, but rather represent different interactions: charge-transfer association, ionic salt formation and host–guest inclusion. Their pharmaceutical relevance depends on the endpoint measured: structural organisation, solubility, dissolution or assay performance. Representative triamterene complex systems and their reported applications are summarised in Table 1.

Table 1. Representative triamterene complex systems and pharmaceutical applications

System	Preparation or study	Characterisation	Principal finding	Ref.
Complex salts in acidic systems	Phase-solubility investigation	Solubility profiles and composition analysis	Association involving protonated and unprotonated triamterene.	[12]
Carboxylic-acid and API salts or solvates	Liquid-assisted grinding and evaporation	Crystallography and thermal analysis	Diverse hydrogen-bond networks and solid forms, including ibuprofen-containing systems.	[13]
AA and AA2G solid dispersions	Solvent evaporation; 1:1 systems	PXRD, DSC, FTIR and NIR	Approximately 90% dissolved at 3 min versus approximately 30% for triamterene alone.	[14]
SBE-β-CD inclusion system	Mixing, kneading, freeze-drying and mechanical treatment	UV, solution and solid-state NMR, and PXRD	Association constant 510 L/mol; phenyl-ring inclusion and improved dissolution after mechanochemical preparation.	[15]
SCX6 inclusion system	Host–guest association at pH 6.5	Fluorescence, UV–Vis, NMR, FTIR, SEM and DSC	1:1 inclusion complex with increased aqueous solubility.	[16]
TCNQ and DDQ charge-transfer complexes	Donor–acceptor reactions	Spectroscopy and computational calculations	Coloured complexes used for spectrophotometric drug assays.	[17]

AA, ascorbic acid; AA2G, ascorbic acid 2-glucoside; API, active pharmaceutical ingredient; DSC, differential scanning calorimetry; FTIR, Fourier-transform infrared spectroscopy; NIR, near-infrared spectroscopy; NMR, nuclear magnetic resonance; PXRD, powder X-ray diffraction; SBE-β-CD, sulfobutylether-β-cyclodextrin; SCX6, p-sulfonatocalix[6]arene; SEM, scanning electron microscopy; UV–Vis, ultraviolet–visible spectroscopy; TCNQ, 7,7,8,8-tetracyanoquinodimethane; DDQ, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. Results refer to the conditions of the individual studies.

6 PHARMACOLOGICAL AND BIOLOGICAL ACTIVITIES

6.1 Established Diuretic Mechanism and Pharmacokinetics

Triamterene blocks epithelial sodium channels, which decreases electrogenic sodium reabsorption and the driving force for potassium secretion. Experiments with expressed rat channels showed voltage- and pH-dependent blockade, with higher affinity for the protonated compound [1]. The results give a molecular basis for its potassium-sparing diuretic activity.

Both triamterene and its active hydroxylated sulfate metabolite are involved in drug disposition. Hasegawa and colleagues studied their pharmacokinetics in humans, highlighting the need to consider metabolite exposure along with the parent drug [18]. Gilfrich and colleagues compared intravenous and oral administration in a randomised crossover study with six healthy volunteers, and estimated oral bioavailability at 52%, which corresponded to an absorbed fraction of ~83% [19]. This difference was attributed partly to first-pass elimination. The results suggest that dissolution improvement does not necessarily lead to a proportional rise in the amount of parent drug in the circulation.

6.2 Experimental Anticancer Activities and Drug Repurposing

Experimental studies of the anticancer properties of triamterene have been pursued through several mechanisms. Guillotin et al. discovered selective cytotoxicity in DNA mismatch-repair-deficient tumour models [5]. The effect was associated with antifolate activity and was thymidylate synthase dependent, resulting in increased reactive oxygen species and DNA double-strand breaks in susceptible cells. This work connects activity with a defined cellular susceptibility and provides a basis for the evaluation of mismatch-repair status as a possible response biomarker.

To and colleagues explored the use of triamterene as a histone deacetylase inhibitor in cisplatin-resistant non-small cell lung cancer models [6]. Triamterene caused an increase in histone acetylation and facilitated changes involving the promoters of the human copper transporter 1 and p21 genes. These effects were associated with higher accumulation of cisplatin in the cells and with the induction of cell-cycle arrest, DNA damage and apoptosis. Potentiation of cisplatin activity was also noted in a cisplatin-resistant patient-derived xenograft. The results are consistent with a combination-treatment hypothesis, but do not establish efficacy in patients.

There are other studies that have investigated the effects on tumour dissemination and cell viability. Iishi and co-workers found suppression of bombesin-enhanced peritoneal metastasis in rats with azoxymethane-induced intestinal adenocarcinomas, without a corresponding reduction in the tumour-cell proliferation measure [20]. The half-maximal inhibitory concentrations in HCT116 and CT26 colon cancer cells were 31.30 μM and 24.45 μM, respectively, in the study by Hosseinpour Moghadam and colleagues [21]. Supporting experiments demonstrated interactions with calf-thymus DNA and human serum albumin, but these binding data were not sufficient to prove the mechanism of cellular cytotoxicity.

More recently, Barbieri et al. found that triamterene is an inhibitor of chloride intracellular channel 1 in glioblastoma stem-cell models [22]. Electrophysiological measurements were accompanied by decreased proliferation and invasion in culture and antitumour activity in xenografted zebrafish embryos. Triamterene also improved experimental responses to temozolomide and combined radiation–temozolomide treatment. These findings provide further preclinical support for the repurposing of triamterene, which requires demonstration of tumour exposure, target engagement, and an acceptable therapeutic window. Table 2 shows the results of representative studies.

Table 2. Representative studies of triamterene's experimental anticancer activities

Biological focus	Experimental model	Principal finding	Evidence scope	Ref.
Mismatch-repair deficiency	MMR-deficient tumour cells and in vivo models	Selective antifolate-associated cytotoxicity involving thymidylate synthase, oxidative stress and DNA damage.	Preclinical rationale for biomarker-directed investigation.	[5]
Cisplatin resistance	NSCLC cell lines and resistant patient-derived xenograft	HDAC inhibition, increased histone acetylation and cisplatin accumulation, and improved cisplatin response.	Combination activity demonstrated in experimental models.	[6]
Peritoneal metastasis	Rats with azoxymethane-induced intestinal tumours	Reduced bombesin-enhanced metastasis without a corresponding decrease in the proliferation measure.	Specific animal model of tumour dissemination.	[20]
Colon cancer cytotoxicity	HCT116 and CT26 cells; DNA and HSA binding assays	IC_{50} values of 31.30 and 24.45 μM, respectively; supporting DNA and albumin interaction studies.	Cellular potency and binding do not establish a clinical therapeutic window.	[21]
CLIC1 inhibition	Glioblastoma stem-cell cultures and zebrafish xenografts	CLIC1 blockade, reduced proliferation and invasion, and enhanced experimental treatment responses.	Preclinical findings requiring exposure and safety assessment.	[22]

CLIC1, chloride intracellular channel 1; HDAC, histone deacetylase; HSA, human serum albumin; IC_{50}, half-maximal inhibitory concentration; MMR, mismatch repair; NSCLC, non-small cell lung cancer. None of the studies establishes clinical anticancer efficacy.

6.3 Safety and Translational Considerations

Additional constraints for further development are also given by the established pharmacology of triamterene. Walker et al. reported hyperkalaemia after triamterene use in diabetic patients [23]. Nasr and colleagues reported triamterene crystalline nephropathy, in which intrarenal crystal deposition can be related to kidney injury [24]. These observations are important for the development of

formulations or dosing regimens designed to enhance exposure.

Therefore, the concentration needed for an experimental anticancer effect should be evaluated along with renal handling, exposure to active metabolites, and electrolyte effects. There is clinical experience with its existing use as a diuretic, but this does not establish the safety of higher exposures or new combinations in oncology. Formulation and repurposing studies should relate efficacy measurements to pharmacokinetic and safety endpoints, not just increased dissolution or in vitro potency.

7 EVIDENCE GAPS AND FUTURE DIRECTIONS

The chemical and pharmaceutical properties of triamterene should be correlated with measurable improvement in the performance of the drug in future studies. Comparative synthesis studies should be performed under similar conditions and evaluation of yield, impurity profile, solvent consumption and scalability. Salts, solvates and inclusion systems should be evaluated for the stability in storage, reproducibility of preparation and dissolution in physiologically relevant media. Pharmacokinetic evaluation is needed to determine whether there is an increased or consistent exposure with enhanced dissolution. For biological investigations, use of complementary experimental models to demonstrate target engagement, target selectivity, and concentration–response relationships. Unbound drug concentrations and active metabolites should be given special consideration. Activity should be demonstrated at exposure levels that are compatible with renal and electrolyte safety for anticancer development, and biomarkers identified that can predict response to activity. Structural characterization and formulation studies coupled with exposure related biological testing would provide a better basis for selecting triamterene systems or derivatives for further development.

8 CONCLUSION

The diuretic effect of Triamterene is well recognized and its pteridine structure is flexible. It is possible to obtain the parent compound and variants of the structure by synthetic chemistry and to modify the pharmaceutical properties by salt formation, inclusion systems and other intermolecular associations. Experimental studies have also resulted in the discovery of biological activities to be further investigated, particularly in cancer models. However, optimization of formulation and confirmation of the preclinical activity is required by pharmacokinetic and safety studies. Chemical characterisation and exposure–response relationships should be added to future development to determine whether or not these techniques offer clinically meaningful benefits.

REFERENCES

1. Busch AE, Suessbrich H, Kunzelmann K, Hipper A, Greger R, Waldegger S, et al. Blockade of epithelial Na^+ channels by triamterenes—underlying mechanisms and molecular basis. Pflugers Arch. 1996;432(5):760–766. https://doi.org/10.1007/s004240050196

2. Hughes DS, Delori A, Rehman A, Jones W. Using crystallography, topology and graph set analysis for the description of the hydrogen bond network of triamterene: a rational approach to solid form selection. Chem Cent J. 2017;11:63. https://doi.org/10.1186/s13065-017-0293-1

3. Li AY, Xu LL, Chen JM, Lu TB. Solubility and dissolution rate enhancement of triamterene by a cocrystallization method. Cryst Growth Des. 2015;15(8):3785–3791. https://doi.org/10.1021/acs.cgd.5b00439

4. Mukne AP, Nagarsenker MS. Triamterene-β-cyclodextrin systems: preparation, characterization and in vivo evaluation. AAPS PharmSciTech. 2004;5(1):E19. https://doi.org/10.1208/pt050119

5. Guillotin D, Austin P, Begum R, Freitas MO, Merve A, Brend T, et al. Drug-repositioning screens identify triamterene as a selective drug for the treatment of DNA mismatch repair deficient cells. Clin Cancer Res. 2017;23(11):2880–2890. https://doi.org/10.1158/1078-0432.CCR-16-1216

6. To KKW, Cheung KM, Cho WCS. Repurposing of triamterene as a histone deacetylase inhibitor to overcome cisplatin resistance in lung cancer treatment. J Cancer Res Clin Oncol. 2023;149(10):7217–7234. https://doi.org/10.1007/s00432-023-04641-1

7. Peng B, Zhang Z, Wang JR, Li M, Zhang Q, Mei X. Confocal Raman micro-spectral evidence and physicochemical evaluation of triamterene salts. Analyst. 2019;144(2):530–535. https://doi.org/10.1039/C8AN01579A

8. Dahl O, Ziedrich KH, Marek GJ, Paradies HH. Physicochemical and structural studies of triamterene. J Pharm Sci. 1989;78(7):598–606. https://doi.org/10.1002/jps.2600780719

9. Spickett RGW, Timmis GM. The synthesis of compounds with potential anti-folic acid activity. Part I. 7-Amino- and 7-hydroxy-pteridines. J Chem Soc. 1954:2887–2895. https://doi.org/10.1039/JR9540002887

10. Weinstock J, Dunoff RY. Pteridines. IX. Some pteridine isomers of triamterene. J Med Chem. 1968;11(3):565–568. https://doi.org/10.1021/jm00309a033

11. Graboyes H, Jaffe GE, Pachter IJ, Rosenbloom JP, Villani AJ, Wilson JW, et al. Pteridines. X. Some pyrimidopyrimidine isomers of triamterene. J Med Chem. 1968;11(3):568–573. https://doi.org/10.1021/jm00309a034

12. Dittert LW, Higuchi T, Reese DR. Phase solubility technique in studying the formation of complex salts of triamterene. J Pharm Sci. 1964;53(11):1325–1328. https://doi.org/10.1002/jps.2600531108

13. Rehman A, Delori A, Hughes DS, Jones W. Structural studies of crystalline forms of triamterene with carboxylic acid, GRAS and API molecules. IUCrJ. 2018;5(3):309–324. https://doi.org/10.1107/S2052252518003317

14. Onoda H, Inoue Y, Ezawa T, Murata I, Chantadee T, Limmatvapirat S, et al. Preparation and characterization of triamterene complex with ascorbic acid derivatives. Drug Dev Ind Pharm. 2020;46(12):2032–2040. https://doi.org/10.1080/03639045.2020.1842439

15. Maeda H, Shiobara R, Tanaka M, Kajinami A, Nakayama H. Effect of mechanochemical inclusion of triamterene into sulfobutylether-β-cyclodextrin and its improved dissolution behavior. Drug Dev Ind Pharm. 2021;47(4):535–541. https://doi.org/10.1080/03639045.2020.1850759

16. Chao J, Zhang Y, Fan X, Wang H, Li Y. Investigation of the inclusion interaction of p-sulfonatocalix[6]arene with triamterene. Spectrochim Acta A Mol Biomol Spectrosc. 2013;116:295–300. https://doi.org/10.1016/j.saa.2013.07.03217. Aldawsari FS, Albugami FS, Altalhi TA, Refat MS, Shakya S, Adam AMA, et al. Spectroscopic measurements, computational calculations, and drug assay applications of charge-transfer complexes comprising the pharmaceutical triamterene and the organic acceptors TCNQ and DDQ. Bull Chem Soc Ethiop. 2025;39(10):1961–1975. https://doi.org/10.4314/bcse.v39i10.7

18. Hasegawa J, Lin ET, Williams RL, Sörgel F, Benet LZ. Pharmacokinetics of triamterene and its metabolite in man. J Pharmacokinet Biopharm. 1982;10(5):507–523. https://doi.org/10.1007/BF01059034

19. Gilfrich HJ, Kremer G, Möhrke W, Mutschler E, Völger KD. Pharmacokinetics of triamterene after i.v. administration to man: determination of bioavailability. Eur J Clin Pharmacol. 1983;25(2):237–241. https://doi.org/10.1007/BF00543797

20. Iishi H, Tatsuta M, Baba M, Uehara H, Nakaizumi A, Akedo H. Triamterene suppresses bombesin-enhanced peritoneal metastasis of intestinal adenocarcinomas induced by azoxymethane. Jpn J Cancer Res. 1996;87(7):730–734. https://doi.org/10.1111/j.1349-7006.1996.tb00285.x

21. Hosseinpour Moghadam N, Salehzadeh S, Tanzadehpanah H, Saidijam M, Karimi J, Khazalpour S. In vitro cytotoxicity and DNA/HSA interaction study of triamterene using molecular modelling and multi-spectroscopic methods. J Biomol Struct Dyn. 2019;37(9):2242–2253. https://doi.org/10.1080/07391102.2018.1489305

22. Barbieri F, Cianci F, Tremonti BF, Dellacasagrande I, Corsaro A, Rey G, et al. Repurposing triamterene as chloride intracellular channel 1 inhibitor via ligand-based approach for glioblastoma. Mol Ther. 2026;34(10):6086–6110. https://doi.org/10.1016/j.ymthe.2026.07.035

23. Walker BR, Capuzzi DM, Alexander F, Familiar RG, Hoppe RC. Hyperkalemia after triamterene in diabetic patients. Clin Pharmacol Ther. 1972;13(5 Pt 1):643–651. https://doi.org/10.1002/cpt1972135part1643

24. Nasr SH, Milliner DS, Wooldridge TD, Sethi S. Triamterene crystalline nephropathy. Am J Kidney Dis. 2014;63(1):148–152. https://doi.org/10.1053/j.ajkd.2013.06.023