DOI 10.5281/twist.10049652#490

TWIST, 2025, Vol. 20, Issue 3, pp. 349-356

TWIST

Journal homepage: www.twistjournal.net

Preparation and Characterization, ^{99m}Tc-Taurine Complex as a Novel SPECT Cancer Imaging Agent

Ahmed S. El-Kholany*
Medical Laboratory Department, Faculty of Applied Health Sciences Technology,
Pharos University in Alexandria, Alexandria, Egypt
[**Corresponding author*]

Hesham M. Kamel
Medical Laboratory Department, Faculty of Applied Health Sciences Technology,
Pharos University in Alexandria, Alexandria, Egypt

Abstract
Cancer remains a main cause of world mortality, with early detection being crucial for powerful treatment and stepped forward affected person effects. This study focuses on the preparation and characterization of technetium-taurine complex, specifically ^{99m}Tc-taurine, as radiopharmaceutical with high cancer imaging potential. The goal was to synthesize the complex, determine its structure. The complex characterized by infrared (IR) spectroscopy, proton nuclear magnetic resonance (^{1}H NMR), liquid chromatography–mass spectrometry (LC-MS), and high-performance liquid chromatography (HPLC), all of which confirmed the formation of the complex. Molecular docking study is done for Taurine and Tc-Taurine showed that Both Taurine and Tc-Taurine Complex show binding affinity to aromatase (3S7S). and Tc-Taurine complex could be explored for SPECT imaging in breast cancer, particularly for detecting aromatase (3S7S)-expressing tumors.

Keywords
Taurine, ^{99m}Tc complexes, Spectroscopy, Molecular Docking

INTRODUCTION

Taurine is a obviously occurring sulfur-containing amino acid-like compound observed abundantly in mammalian tissues such as the brain, coronary heart, retina, and skeletal muscle tissues. Although it isn't incorporated into proteins, taurine plays crucial physiological roles which include bile acid conjugation, osmoregulation, membrane stabilization, calcium signaling, neuromodulation, and antioxidative defense mechanisms [1].

Taurine famous cytoprotective, antioxidant, and anti-inflammatory residences. It has been shown to enhance mitochondrial feature, reduce oxidative stress, beautify antioxidant enzyme expression, and adjust redox-touchy transcription elements along with Nrf2 [2]. These consequences contribute to cardiovascular health, neuroprotection, and anti-getting older mechanisms [3].

Cancer stays a main cause of worldwide mortality, with early detection being vital for powerful remedy and improved affected person effects [4]. In nuclear remedy, technetium-99m (^{99m}Tc) has emerged as the radionuclide of desire for diagnostic imaging because of its choicest physical properties (140 keV gamma emission, 6-hour half-existence) and cost-effective manufacturing from 99Mo/99mTc generators [5]. The development of novel 99mTc-based absolutely radiopharmaceuticals concentrated on tumor-specific metabolic pathways is an lively region of research to decorate diagnostic accuracy [6]

Taurine (2-aminoethanesulfonic acid) is a truly going on amino sulfonic acid located abundantly in mammalian tissues, wherein it plays vital roles in osmoregulation, antioxidation, calcium signaling, and membrane stabilization [11]. Its organic results are multifaceted, which includes modulation of inflammation, safety against oxidative strain, and regulation of apoptosis, which might be all applicable to cancer biology [9,11].

Biological Effects of Taurine:

Taurine acts as a strong antioxidant, scavenging reactive oxygen species (ROS) and enhancing the interest of endogenous antioxidant enzymes including superoxide dismutase and glutathione peroxidase [10,11]. This antioxidative capacity helps defend cells from oxidative injury, a procedure implicated in each cancer initiation and progression. Taurine also modulates immune responses and supports cell homeostasis, contributing to its cytoprotective effects [11].

Role in Cancer Treatment

Research demonstrates that taurine possesses antitumor houses in numerous maximum cancers kinds, alongside colon, lung, breast, and prostate cancers. It can inhibit most cancers cellular proliferation and result in apoptosis thru more than one mechanism, alongside upregulating seasoned-apoptotic proteins (e.G., PUMA, Bax) and downregulating anti-apoptotic proteins (e.G., Bcl-2), regularly thru mitochondrial and JNK signaling pathways. Taurine's anti-inflammatory results, specially through the inhibition of NF-κB-mediated pathways, in addition make contributions to its tumor-suppressive moves [7]. Additionally, taurine has been established to decorate the efficacy of chemotherapeutic dealers and mitigate their factor effects, which includes reducing drug-prompted toxicity and enhancing immune function all through maximum cancers remedy. For instance, taurine supplementation can alleviate chemotherapy-induced complications and might help triumph over drug resistance, making it a promising adjunct in most cancers remedy regimens [9-13].

However, the role of taurine in cancer is complicated. Some studies endorse that high taurine levels may additionally sell tumor increase in certain contexts, along with lung most cancers, whilst additionally assisting the survival and characteristic of anti-tumor immune cells like CD8 T cells [8]. The net impact of taurine can also rely on the tumor kind, microenvironment, and immune repute of the host.

The improvement of powerful radiopharmaceuticals for cancer imaging stays a crucial region in nuclear remedy, with technetium-99m (^{99m}Tc) complexes playing a pivotal function due to their favorable bodily and chemical homes. ^{99m}Tc gives an ideal half of-life of approximately 6 hours and emits gamma photons appropriate for Single Photon Emission Computed Tomography (SPECT), making it extensively used for diagnostic imaging. Among diverse ^{99m}Tc-labeled marketers, complexes concentrated on particular tumor markers have shown promising results in enhancing cancer detection and staging accuracy.

Taurine, a clearly happening amino acid by-product, has attracted hobby as a ligand for ^{99m}Tc because of its organic compatibility and potential tumor-concentrated on residences. The ^{99m}Tc-Taurine complicated is being explored as a novel SPECT imaging agent for most cancers, aiming to mix the focused on talents of taurine with the imaging blessings of ^{99m}Tc. This method aligns with contemporary advances in ^{99m}Tc-categorized compounds such as ^{99m}Tc-PSMA for prostate most cancers and ^{99m}Tc-FAPI for fibroblast activation protein imaging, which have examined excessive sensitivity and specificity in detecting number one and metastatic lesions. [14-16]

The use of ^{99m}Tc-Taurine could potentially improve tumor visualization by using exploiting biochemical pathways precise to most cancers' cells, thereby offering precious diagnostic statistics to manual treatment. Given the developing proof assisting ^{99m}Tc-based radiopharmaceuticals in oncology, in addition research into the ^{99m}Tc-Taurine complicated could extend the arsenal of effective SPECT imaging marketers for most cancers control.

The targets of this paintings are:

1. To synthesize ^{99m}Tc-taurine complex.
2. To determine the structural of the prepared compound using different spectroscopic techniques.
3. Evaluate the binding affinity of both taurine and ^{99m}Tc-taurine to the human placental aromatase enzyme (3S7S) using molecular docking simulations to predict their inhibitory potential.

If demonstrated, this complex ought to offer a flexible, fee-effective diagnostic tool for SPECT-primarily based most cancers detection throughout more than one tumor types.

EXPERIMENTAL

Preparation the complex

The reduction of Tc, an important transition metal, turned into executed thru the addition of tin chloride, a normally used lowering agent. This reduction technique was executed inside the presence of ascorbic acid, a acknowledged antioxidant that enables to facilitate the response. Following the reduction step, the Tc ions had been then capable of shape a complicated with Taurine.

Infrared spectra

The series of information was achieved the use of the Shimadzu 4800s FTIR spectrometer Maxima, that is a renowned tool manufactured in Japan. This instrumental evaluation changed into accomplished at the Central Laboratory of the Faculty of Sciences at Alexandria University, a prestigious academic institution regarded for its scientific studies endeavors.

HPLC Chromatographic

A novel and complex approach, particularly excessive-performance liquid chromatography (HPLC), has been meticulously designed and applied for the motive of appropriately quantifying the presence of Taurine as well as the Tc-Taurine complex. The HPLC system utilized on this take a look at changed into composed of a modern C18 column,

which performed a pivotal position in the separation and analysis of the focused compounds. The solvent device employed was a meticulously balanced combo of phosphorus acid 0.1% and acetonitrile, with a selected ratio of 15:85, ensuring top of the line performance and efficiency. Furthermore, the flowrate of the machine changed into exactly set at 0.5 ml/min, which facilitated the smooth and continuous movement of the analytes thru the column. Lastly, to efficiently discover and quantify the compounds of hobby, a exceptionally sensitive UV detector running at an most appropriate wavelength of 254 nanometers, turned into deployed to make certain correct and reliable effects turned into integrated into the system. This modern gadget was expertly utilized by the esteemed Central Laboratory Faculty of Sciences at Alexandria University, similarly validating the credibility and reliability of the findings received.

LCMS Mass spectra

The analysis of the sample was performed using liquid chromatography–electrospray ionization–tandem mass spectrometry (LC-ESI-MS/MS) with an ExionLC AC system (USA) for separation and SCIEX Triple Quad 5500+ MS/MS system (Singapore) equipped with an electrospray ionization (ESI) for detection.

HPLC and LCMS have been done per week after getting ready the complicated, which suggests the steadiness of the organized complex.

1HNMR measurements

H Nuclear Magnetic Resonance (NMR) spectra have been recorded DMSO-d6 at 500 MHz on a JNM-ECZ500R

Molecular docking

The simulated interaction of designed drug with the protein structure of selected pathogens was modeled by MOE 2015.10 program. The 3D crystal structure of the selected proteins was obtained from the Protein Data Bank (PDB). The inhibition efficiency of the designed drugs is evaluated by the strength of interactions with the target proteins, which was predicted from the scoring energy and the length of the H-bonds in the docked complex. removal of water molecules, atomic charges clarifying, and then energy minimization by MMFF94x force field .10 Poses of interactions were recorded for each species, where the best pose with the shortest ligand-receptor distance and the highest scoring

RESULTS AND DISCUSSIONS

Infrared spectra of Taurine and Tc-Taurine complex

The IR spectra of taurine and the Tc-taurine complex (Figure 1, Table 1) discovered that the N–H stretching band at 3208 cm^{-1} in free taurine broadened upon complexation. The band at 3441 cm^{-1} of the complex spectrum corresponds to O–H stretching vibrations, along with a shift within the N–H band due to the coexistence of the two groups within the Tc-taurine complex. The shift within the S=O stretching band (1618 → 1628 cm^{-1}) suggests the involvement of the sulfonic institution in complexation [17–18]. Meanwhile, the C–S band at 1307 cm^{-1} shifted barely to 1301 cm^{-1}, probable because of its proximity to the coordination site. Minimal adjustments in C–S–O vibrations imply that these companies are not primary coordination sites, which is consistent with taurine's metal-binding behavior. The new band 1467 cm^{-1} New band likely corresponds to altered bonding modes in the complex

The presence of M–O and M-N bands at 528 and 471 respectively confirm coordination through the nitrogen atom, which, together with Metal–O bonding, indicates bidentate coordination of taurine through both amino and sulfonic groups [19].

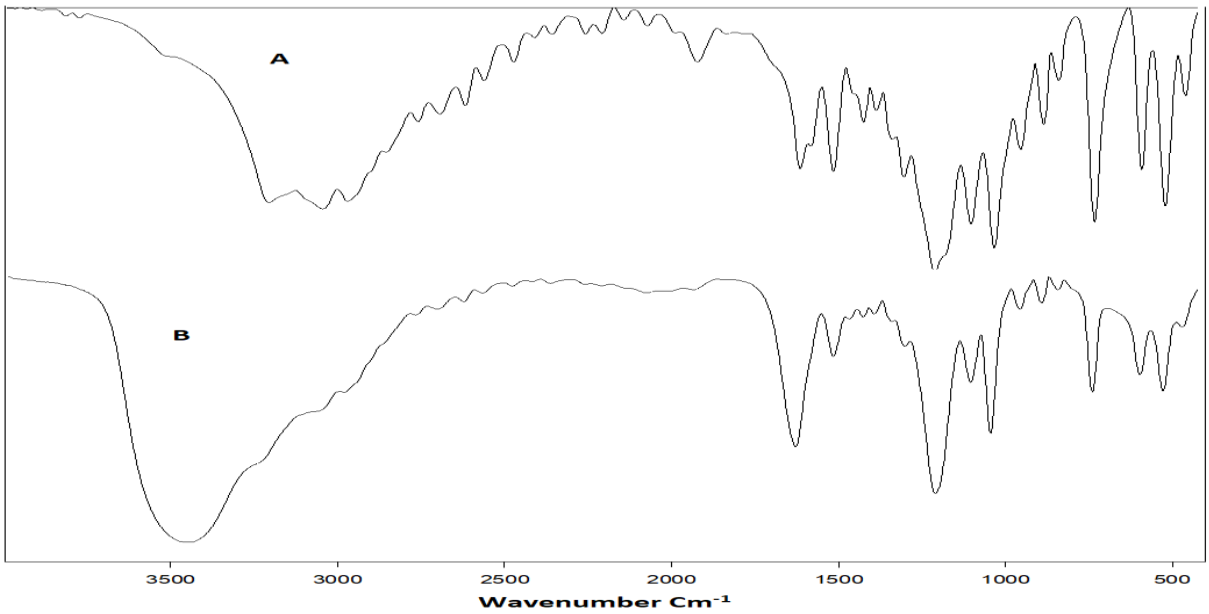

Fig. 1 Infrared spectra of Taurine (A) and Tc- Taurine complex (B)

Table 1 Fundamental infrared bands (cm^{-1}) of Taurine and Tc- Taurine complex in aqueous solution

Vibrational Mode	Taurine	Tc-Taurine
$\nu_{N–H}$, $\nu_{O–H}$	3208	3441
$\nu_{S=O}$	1618	1628
$\nu_{C–S}$	1307–1215	1301–1209
$\nu_{C–S–O}$	957	956
$\nu_{Metal–O}$	–	528
$\nu_{Metal–N}$	–	471

^{1}H-NMR Spectra

The ^{1}H NMR spectrum of taurine presentations a multiple peak at δ 3.00 ppm, assigned to the methylene protons adjacent to the sulfonic acid organization (–CH_2–SO_3H), and some other multiple at δ 2.68 ppm, similar to the methylene protons adjoining to the amine institution (–CH_2–NH_2). Additional signals at δ 3.36 and a couple of 2.46 ppm are attributed to the zwitterionic shape of taurine, which alters the electron distribution and therefore affects the chemical shifts. Peaks found at δ 7.60 ppm and δ 1.19 ppm are assigned to the exchangeable protons of the sulfonic group and amine organizations, respectively. The disappearance of the band that refers to the proton of the sulfonic group in the ^{1}H NMR spectrum of Taurine-Tc Complex prove the formation of Tc-O coordination bond, while the small shifts of the two methylene groups in the complex is strong evidence for the participation of both the sulfonic and the amine group in complexation, (Figure **3**, Table 2).

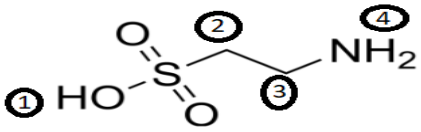

Fig. 2 Taurine Structure

Table 2 ^{1}H NMR (PPM) of Taurine and Tc- Taurine complex in aqueous solution

	1	2	3	4
Taurine	7.613	3.00–3.31	2.45–2.70	1.19
Taurine-Tc Complex	-	2.91-2.97	2.46-2.72	1.19

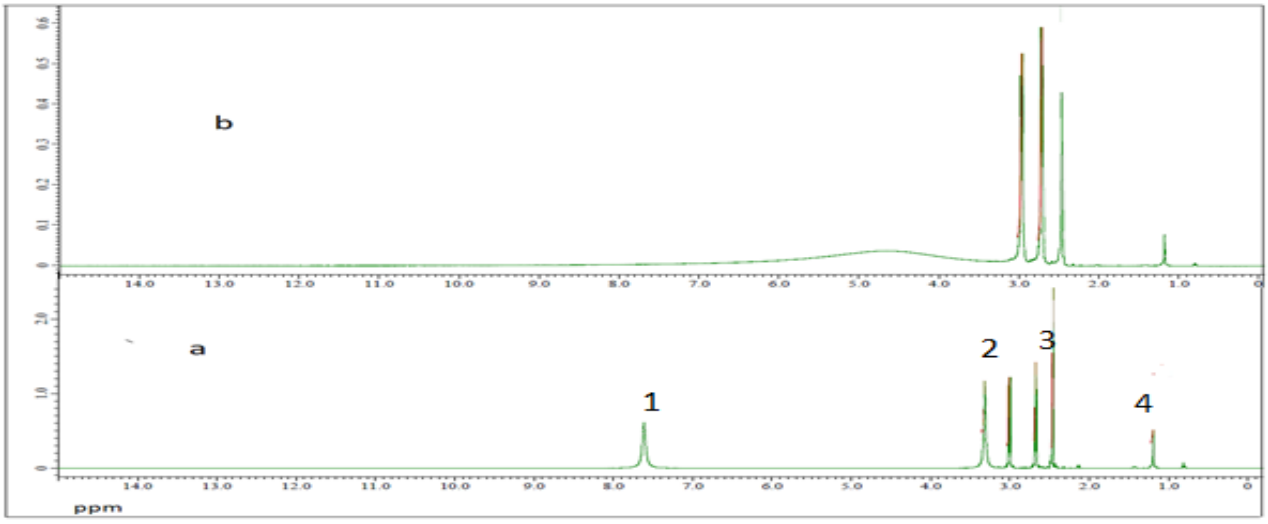

Fig. 3 ^{1}H NMR of Taurine (a) and Tc- Taurine complex (b)

HPLC Chromatographic

The HPLC analysis, which was conducted for Taurine as a stander and the solution resulting from the reaction of Taurine and Tc, as depicted in Figure (A, B), The appearance of the band for the Tc- Taurine complex at a retention time (3.779 min) is considered conclusive evidence of the formation of a stable complex, as this analysis was conducted several days after the reaction.

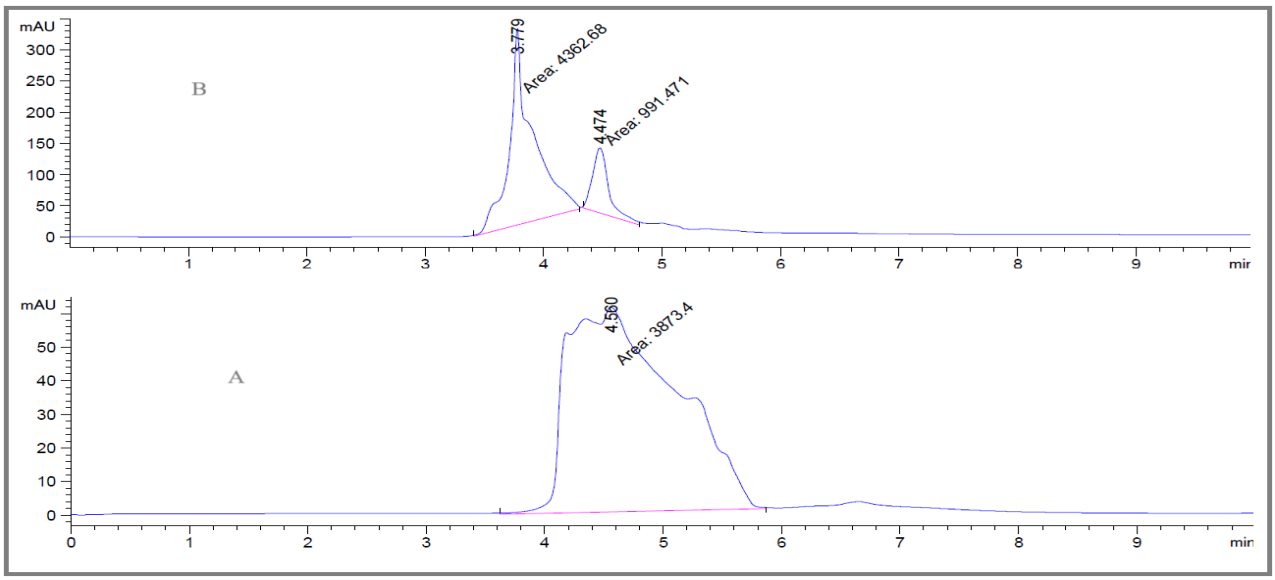

Fig. 6 HPLC spectrum for A) Taurine B) Tc- Taurine complex

Table 3 HPLC data for Taurine and Tc- Taurine complex

Peak	Retention time(min)	Area	Area %
Taurine	4.5	991.47101	18.5178
Tc- Taurine	3.779	4362.68115	81.4822

LCMS Mass spectra

A meticulous exam of the high-quality-mode mass spectrum of the technetium–taurine complex, as illustrated in Figure 4, shows more than one awesome peaks, every corresponding to mass-to-charge (m/z) ratios. Among these, distinguished peaks are especially noteworthy. The first, at m/z 274.08, corresponds to the intact Tc–taurine complex ion. Other notable peaks at m/z 256.10, 230.10, 212.10, 106.08, and 102.07 represent the complex after losing various groups during mass spectrometry ionization. Detailed spectral analysis shows that the molecular formulation of the intact complex is $[TcC_2H_8O_6NS]$, which can be represented as [Tc (Taurine)(O)$(OH)_2$].

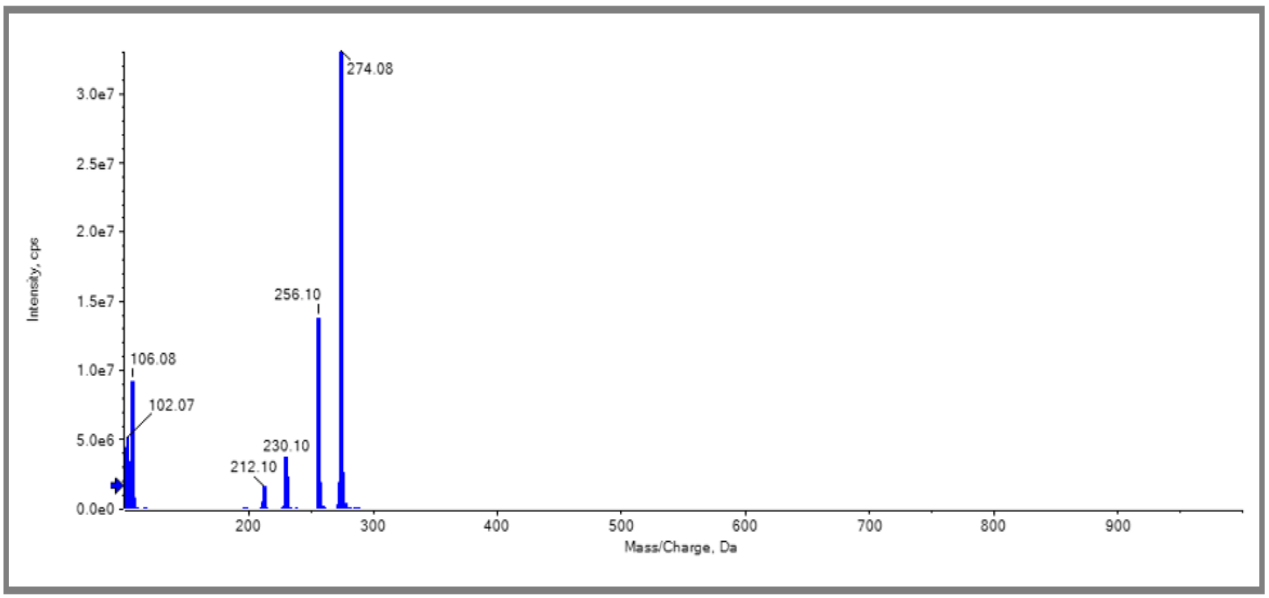

Fig. 4 LCMS Mass spectra Tc-Taurine complex

Based on the spectroscopic data, the Tc-Taurine complex its noticed that:

- Taurine coordinated as a bidentate ligand through both the amino nitrogen and sulfonate oxygen
- Possible structure: [TcO(taurine)$(OH)_2$], with taurine forming a Six-membered chelate ring

Molecular docking

The selected protein 3s7s represents the crystal structure of the human placentalany proposed biologically active compound. This approach elucidates the ligand-receptor site and type of interactions. It also givesan estimation of the distance between the ligand and the receptor inside the interaction grid. The scoring energy of each pose simulated by the docking calculations reflects the degree of inhibition effect of the corresponding ligand. In the present study, the selected

protein 3s7s represents the crystal structure of the human placental aromatase enzyme that catalyzes the synthesis of estrogen hormone and contributes to estrogen-dependent breast cancer 50. All ligands possess an appreciable extent of interactions with the receptor protein based on the scoring energy . The result show the abibilty of Taurine to inhibt 3s7s protien.

The docked Taurine, (Figures 5,6), have effective ligand-receptor interaction distances were ≤ 3.5 A in most cases, which indicates the presence of typical real bonds and hence high binding affinity. For example, the nearest interaction is observed *via* H-donors with 3S7S (2.66A) Taurine Furthermore, binding sites were observed of different amino acids (Gln 218 ,Asp 222,Arg 102, and Asp 309) with ligand demonstrating their high inhibition with Moldock score -36.02

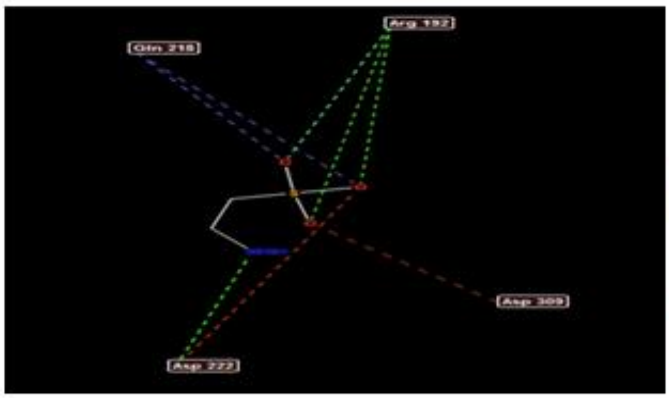

Fig.5 2D structure of Molecular docking of Taurine with 3s7s protein

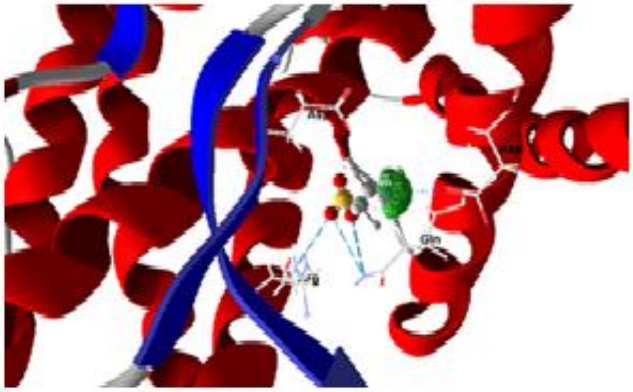

Fig. 6 Virtual Molecular docking of the best docked Taurine with 3s7s

Tc-Taurine Complex

The docked Tc-Taurine Complex , Figures (7,8), have effective ligand-receptor interaction distances were ≤ 3.5 A in most cases, which indicates the presence of typical real bonds and hence high binding affinity . For example, the nearest interaction is observed *via* H-donors with 3S7S (2.66A) and Tc-Taurine Complex Furthermore, eight binding sites were observed of different amino acids(Trp 141,Arg 116,Arg 426, Arg 146, lle 132 and lle 133) with Tc-Taurine Complex demonstrating their high inhibition with Moldock score -63.04 which is an indication for highest inhibition

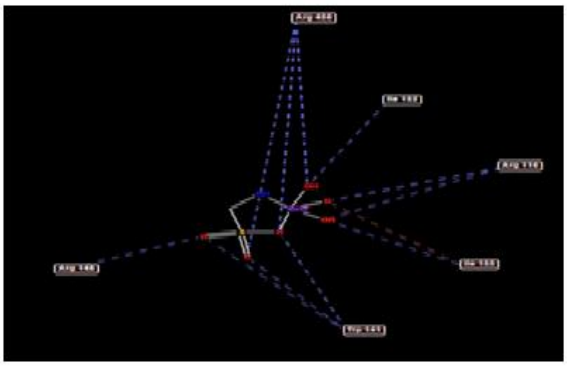

Fig. 7 2D structure of Molecular docking of Tc-Taurine Complex with 3s7s protein

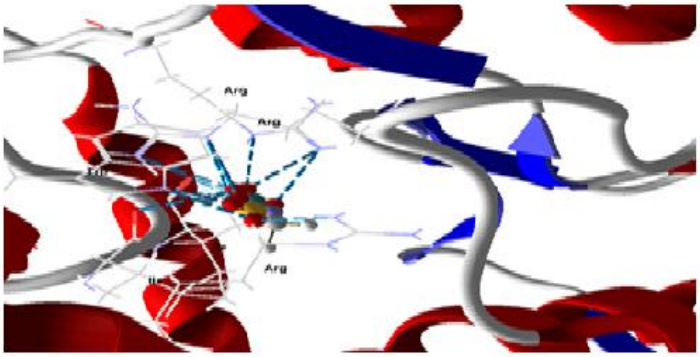

Fig. 8 Virtual Molecular docking of the best docked Tc-Taurine Complex with 3s7s

From the Molecular docking, Tc-Taurine complex could be used for SPECT imaging in breast cancer, particularly for detecting aromatase (3S7S)-expressing tumors.

Since the docking study shows strong binding of Tc-Taurine to 3S7S (aromatase), it could selectively accumulate in estrogen-dependent breast cancer cells, where aromatase is overexpressed and could be used for SPECT imaging in breast cancer.

Table 4 Comparison with Existing Breast Cancer Tracers

Tracer	Target	Imaging Modality	Advantages	Limitations
^{18}F-FDG	Glucose metabolism	PET	Widely used, high sensitivity	Low specificity for hormone-dependent cancers
^{99m}Tc-Sestamibi	Mitochondrial uptake	SPECT	Approved for breast imaging	Non-specific, high muscle uptake
^{68}Ga-DOTA-TATE	Somatostatin receptors	PET	Useful in neuroendocrine tumors	Not for aromatase+ breast cancer
Proposed Tc-Taurine	Aromatase (3S7S)	SPECT	Potentially specific for estrogen+ tumors	

CONCLUSION

This study successfully synthesized and characterized ^{99m}Tc-taurine, demonstrating its high binding affinity to aromatase (3S7S) via molecular docking. The complex's stability and target specificity position it as a promising SPECT tracer for ER+ breast cancer detection.

FUNDING INFORMATION

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

DECLARATION OF CONFLICT

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

ACKNOWLEDGMENTS

The authors would like to thank their students who participated with them in preparing this research, namely Ehdaa El Smahy, Noreen Osman, Noreen Amr Shaat, Malak Hanafy, Noura El Said, Sabah Hossam and Shaban Abd El Aziz.

REFERENCES

1. Huxtable RJ. Physiological actions of taurine. Physiological reviews. 1992 Jan 1;72(1):101-63. https://pubmed.ncbi.nlm.nih.gov/1724621/
2. Seol SI, Kang IS, Lee JS, Lee JK, Kim C. Taurine Chloramine-Mediated Nrf2 Activation and HO-1 Induction Confer Protective Effects in Astrocytes. Antioxidants. 2024 Jan 29;13(2):169.https://doi.org/10.3390/antiox13020169
3. Santulli G, Kansakar U, Varzideh F, Mone P, Jankauskas SS, Lombardi A. Functional role of taurine in aging and cardiovascular health: an updated overview. Nutrients. 2023 Jan;15(19):4236.https://doi.org/10.3390/nu15194236
4. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2021 May;71(3):209-49.https://pubmed.ncbi.nlm.nih.gov/33538338/
5. Jurisson SS, Lydon JD. Potential technetium small molecule radiopharmaceuticals. Chemical Reviews. 1999 Sep 8;99(9):2205-18.https://pubmed.ncbi.nlm.nih.gov/11749479/
6. Liu S, Edwards DS. ^{99m}Tc-labeled small peptides as diagnostic radiopharmaceuticals. Chemical reviews. 1999 Sep 8;99(9):2235-68. https://pubmed.ncbi.nlm.nih.gov/11749481/
7. Adhish M, Manjubala I. An in-silico approach to the potential modulatory effect of taurine on sclerostin (SOST) and its probable role during osteoporosis. Journal of Biomolecular Structure and Dynamics. 2024 Nov 21;42(17):9002-17. https://pubmed.ncbi.nlm.nih.gov/37608541/
8. Song X, Yuan B, Zhao S, Zhao D. Effect of taurine on the proliferation, apoptosis and MST1/Hippo signaling in prostate cancer cells. Translational Cancer Research. 2022 Jun;11(6):1705. https://pubmed.ncbi.nlm.nih.gov/35836537/
9. Baliou S, Kyriakopoulos AM, Spandidos DA, Zoumpourlis V. Role of taurine, its haloamines and its lncRNA TUG1 in both inflammation and cancer progression. On the road to therapeutics. International journal of oncology. 2020 Jul 14;57(3):631-64. https://pubmed.ncbi.nlm.nih.gov/32705269/
10. Tu S, Zhang XL, Wan HF, Xia YQ, Liu ZQ, Yang XH, Wan FS. Effect of taurine on cell proliferation and apoptosis human lung cancer A549 cells. Oncology letters. 2018 Apr;15(4):5473-80. https://pubmed.ncbi.nlm.nih.gov/29552188/
11. Ma N, He F, Kawanokuchi J, Wang G, Yamashita T. Taurine and its anticancer functions: in vivo and in vitro study. Taurine 12: A Conditionally Essential Amino Acid. 2022 Jul 27:121-8. https://pubmed.ncbi.nlm.nih.gov/35882787/
12. Flemming A. Tumour cell consumption of taurine exhausts CD8+ T cells. Nature Reviews Immunology. 2024 May;24(5):306-. https://pubmed.ncbi.nlm.nih.gov/38632489/
13. Wang G, Ma N, He F, Kawanishi S, Kobayashi H, Oikawa S, Murata M. Taurine Attenuates Carcinogenicity in Ulcerative Colitis-Colorectal Cancer Mouse Model. Oxidative medicine and cellular longevity. 2020;2020(1):7935917. https://pubmed.ncbi.nlm.nih.gov/32566100/
14. Wang Q, Ketteler S, Bagheri S, Ebrahimifard A, Luster M, Librizzi D, Yousefi BH. Diagnostic efficacy of [^{99m}Tc] Tc-PSMA SPECT/CT for prostate cancer: a meta-analysis. BMC cancer. 2024 Aug 8;24(1):982. https://pubmed.ncbi.nlm.nih.gov/39118101/
15. Wang T, Zhao L, Qiao W, Sun N, Zhao J, Xing Y. The efficacy of 99mTc-HYNIC-PSMA SPECT/CT in detecting primary lesions and metastasis in newly diagnosed prostate cancer. Frontiers in Oncology. 2023 Jun 2;13:1165694. https://pubmed.ncbi.nlm.nih.gov/37333816/
16. Sun D, Ma L, Liu Y, Bao C, Jia G, Wang T, Wang Y. 99mTc-FAPI-04 SPECT/CT outperforms contrast-enhanced CT in detecting metastasis in postoperative patients with colorectal cancer. Frontiers in Medicine. 2024 Sep 23;11:1462870. https://pubmed.ncbi.nlm.nih.gov/39376651/

17. Ma G, Sun N, Yu Q, Han L, Wu L, Cao H, Han G. Characterization of separation and purification technology and identification of taurine from the bovine liver. Food Analytical Methods. 2018 Feb;11:415-25.
18. Tian F, Li SY. Study of Spectrophotometric Characteristics of the Charge Transfer Complex of Taurine Drug with 7, 7, 8, 8-Tetracyanoquinodimethane. Química Nova. 2020 Sep 15;43(9):1205-9.
19. Abdou S, Abd El-Wahed MM, El Kadi NM, Kolkaila SA, Samy M. Novel Metal Complexes of Bioactive Amide Ligands as New Potential Antibreast Cancer Agents. TWIST. 2023 Dec 10;18(4):151-69.