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Investigation of the Proliferation Effect of Quinine on Rhabdomyosarcoma Cell Line by Using Cytotoxic Activities and Molecular Docking Techniques

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Abstract: Quinine, a classic antimalarial agent, in recent years has attracted attention for its anticancer activity. In this study, we examined the cytotoxic and anti-proliferative effects of Quinine against the Rhabdomyosarcoma (RD) cell line and an exploration of its interaction with the major proteins overexpressed in this cancer. Cytotoxic activity was evaluated using the MTT assay, which indicated a dose-dependent, significant inhibition of RD cell growth, as represented by an IC_{50} value of 39.3µg/ml at a 24-hour treatment time. Morphological changes in line with cytotoxic effect were also observed. Additional molecular docking analysis was also conducted to estimate the binding affinity of Quinine with some proteins implicated in the pathogenesis of Rhabdomyosarcoma. The in silico data showed that Quinine could inhibit the activity of these proteins, and it could be the reason behind its antiproliferative activity. The observation is preliminary evidence of the therapeutic potential of Quinine against Rhabdomyosarcoma and needs more mechanistic and in vivo studies.

Keywords: quinine, Rhabdomyosarcoma, Ic50, Molecular docking.

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Introduction

In the last twenty years, directly from plants approximately 25% of the drugs have been produced, and 25% were chemically developed from natural substances. Plant metabolites can be found in most plant parts such as bark, leaves, flowers, roots, fruits, and seeds since they contain active principles. Plants have been a source of drugs throughout history for centuries, and phytochemicals have played a very crucial role in drug discovery (1,2). Quinine is a naturally occurring alkaloid derived from the bark of *Rauvolfia caffra*, known for its broad spectrum of pharmacological activities, including antipyretic, anti-inflammatory, anti-tumor, and antimalarial effects (3). Its potential in modulating inflammation and inducing programmed cell death has been explored in various human carcinoma cell lines, such as Hep-2 and KB, highlighting its relevance in cancer therapeutics (4). The K562/ADM leukemic cell line demonstrates the *in*

vitro action of Quinine and cinchonine on cytotoxicity and doxorubicin, mitoxantrone, and vincristine uptake. Pharmacokinetics reveals that Quinine must be given before anticancer drugs in clinical trials(5). However, Quinine has a low therapeutic index and is characterized by serious adverse effects (6). The most frequently encountered side effects at therapeutic dosages are combined under the umbrella of cinchonism with mild manifestations including tinnitus, mild impairment in hearing, headache, and nausea. Impairment of hearing is concentration-dependent and reversible (7). Quinine is a bitter, colorless, amorphous powder or crystalline alkaloid, C20 H2 N2O24 H2O, derived from certain cinchona barks and used in medicine to treat malaria (8) and used in tonic water, in which medicinal tonic water was simply carbonated water and a considerable amount of quinine. Nowadays, tonic water for the most part contains a much smaller amount of Quinine and is primarily available for its flavor (9). Rhabdomyosarcoma (RMS) is the most common childhood soft tissue sarcoma, with an annual incidence of (4 to 7) cases per million in children aged less than 15 years. Embryonal Rhabdomyosarcoma (ERMS) is the most common histological subtype, accounting for approximately 60-70% of pediatric cases. In Iraq, the incidence of RMS was around 3% of pediatric cancer in children under 14 years old in 2010 (10). Al-Niaimi (2006) (11) has reported that the incidence of RMS in northern Iraq is approximately 0.8%, in Mosul approximately 2.4% (12), and in Basrah, RMS accounts for approximately 5.94% of cancer cases (13). RMS occurs slightly more in males than in females, with a ratio of (1.3-1.5:1). Furthermore, there has been a slight lower disease prevalence in black and Asian children compared to white children. Some studies have indicated that Rac1, HSP90, P-mTOR, and Bcl-2 proteins are overexpressed in RMS tissues. These proteins seem to play significant roles in the development and growth of RMS (14; 15). This study aimed to evaluate the effect of Quinine on the inhibition of growth in RD cancer cells with a focus on the underlying molecular mechanisms, to explore its potential as an adjunct therapy in cancer treatment.

Methods

Quinine Preparation

Quinine sulfate (Sigma-Aldrich, USA) was used as a reference substance for the current cytotoxicity assays. The compound was of analytical grade, having ≥98% purity, guaranteeing reproducibility of results. A fresh stock solution was made by dissolving the desired quantity in sterile dimethyl sulfoxide (DMSO) followed by a series of dilutions in culture medium to achieve the desired concentrations. The final concentration of DMSO was no greater than 0.1% in any treatment group to avoid solvent-mediated cytotoxicity. All operations were carried out under aseptic conditions and were stored in light-protected vials at 4°C until use.

Rhabdomyosarcoma cell (RD)

A cell line passage´s number (10) was kindly provided by Central Public Health Laboratory, Ministry of Health, Baghdad, Iraq. This cell line is an immortal cell used in medical research; it was derived from a biopsy specimen obtained from a pelvic rhabdomyosarcoma of a 7-year-old Caucasian girl (16). RD cells were seeded in a density of 5×104 cell/ml into

sterile culture plate and left overnight for adherence.

MTT Assay

Cytotoxicity was determined for the compound against RD cells with the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay(17). 1 × 10^5 cells/well were plated in 0.2 ml of DMEM/well in 96-well culture plates. The specific doses of Quinine that were used: 0.5, 10, 20, 25, 30, 40, 50, 60, and 70 µg/ml. Each concentration was added to the cultured cells in the plates, and after 24 hours of incubation at 37°C in a humidified atmosphere with 5% CO_2, cell viability was assessed. After the exposure period, the cytotoxic effect of Quinine was evaluated using the MTT assay. The medium was carefully aspirated from the wells after incubation. Each well was washed with normal saline and 20 µl of MTT (5 mg/ml) was added. The plates were incubated for 4-5 hours at a 5% CO2 incubator for cytotoxicity assessment. After incubation, 100 µl of DMSO: isopropanol (1:1) as a solvent was added to all wells and well mixed with a micropipette and left for 45 seconds. The viable cells were seen by the purple color appearance by the development of formazan crystals. The optical densities (OD) of the suspension were determined at 490 nm using DMSO as a blank.

Molecular Docking

The three-dimensional (3D) structure of the Quinine ligand was retrieved from the ZINC20 database (Zinc ID: ZINC000006484901) and prepared for molecular docking studies. The X-ray crystallographic structures of Rac1, HSP90, P-mTOR, and Bcl-2 proteins, with corresponding Protein Data Bank (PDB) IDs 3TH5, 3QDD, 4JVS, and 2W3I, respectively, were obtained from the RCSB Protein Data Bank (https://www.rcsb.org/). These protein structures were selected based on the following criteria: (i) a resolution of 2 Å or better, (ii) origin from Homo sapiens, and (iii) the presence of a well-defined co-crystallized ligand within the binding site. The crystal structures of the proteins were prepared for docking using AutoDock Vina version 1.1.2, embedded in PyRx version 0.8. Polar hydrogen atoms were added to both the receptor proteins and the ligands to optimize hydrogen bonding interactions during docking simulations. All rotatable bonds in the ligands were set as flexible to allow for conformational sampling, while the receptor proteins were treated as rigid entities. Grid maps were generated using AutoGrid, with the grid boxes centered around the entire receptor structure to encompass the binding sites comprehensively. The docking results were analyzed and visualized using Discovery Studio Visualizer 2020. This process enabled the evaluation of key interactions, such as hydrogen bonds, hydrophobic contacts, and π-π stacking, between the ligand and the target proteins. The binding affinities and molecular orientations derived from the docking studies provided insights into the potential inhibitory mechanisms of the Quinine ligand against the selected proteins.

Statistical analysis

Software Excel 2019 was used in this study. The mean and standard error were assigned.

Result and discussion

In vitro cytotoxicity assessment of Quinine on RD cells

After 24-48 hours, the RD cell line was examined under an inverted microscope. It was found to have pure,

confluent monolayers, free from any fungal or bacterial contamination, as shown by Figure (1A). The effect of Quinine on RD cell viability was assessed by exposing the RD cells to a series of concentrations, and the IC50 concentration after 24 hours of continuous exposure to Quinine in suspension was established. The compound was extremely cytotoxic to the cell line RD and was extremely anti-proliferative in nature. The IC50, which is the concentration of the compound that results in a decrease in absorbance to half of control, was 39.3%, as indicated in Figure (1B) and Table (1). Many researchers have shown interest in examining the use of natural and semi-synthetic compounds in chemotherapy to significantly suppress and inhibit malignant transformation (18,19, 20). In this study, we demonstrated that the natural alkaloid Quinine possesses dose-dependent anti-proliferative action against RD cells. Quinine's anti-proliferative activity was attributed to its alkaloid nature. Alkaloids are one of the most important active components of natural herbs, and some of these molecules have already been used as chemotherapeutic drugs. A good example is camptothecin (CPT), a well-known topoisomerase I (TopI) inhibitor (21,22), and vinblastine, which interacts with tubulin (23). This result was consistent with a previous study by (19) in 2015, research assessed quinine's cytotoxicity on the laryngeal carcinoma cell line (HEp-2) through the MTT assay and apoptosis analysis. The study indicated that Quinine induced programmed cell death, as confirmed by the loss of cell viability, reactive oxygen species modulation, and cell cycle arrest through G0/G1 phase induction in HEp-2 cells. This finding also agreed with a study conducted in 2016 (4), where it was revealed that Quinine could be an effective candidate to suppress cell growth and enhance apoptosis by inhibiting upstream signaling in human Hep-2 laryngeal cancer cells and KB oral cancer cells. And agreed with (24) in 2025 whom suggest that the genes and proteins involved in myogenic differentiation were severely suppressed by Quinine and significantly interfered with muscle regeneration following injury. Based on these observations, Quinine may serve as a potential candidate to prevent cell proliferation and enhance apoptosis via inhibition of up-stream signaling in human Hep-2 laryngeal cancer and KB oral cancer cell.

Table (1): Cytotoxicity of Quinine presented by Mean± SE and GI% values by MTT assay.

Conc. (µg/ml)	Absorbance (Mean± SE)	% inhibition	IC50
0.5	0.405±0.123	19.26	39.3
10	0.370±0.020	26.36	
20	0.336±0.013	33.13	
25	0.320±0.009	36.25	
30	0.280±0.039	44.29	
40	0.252±0.037	49.80	
50	0.232±0.028	53.85	
60	0.186±0.016	62.88	
70	0.1760.013	64.94	
P value: <0.001			

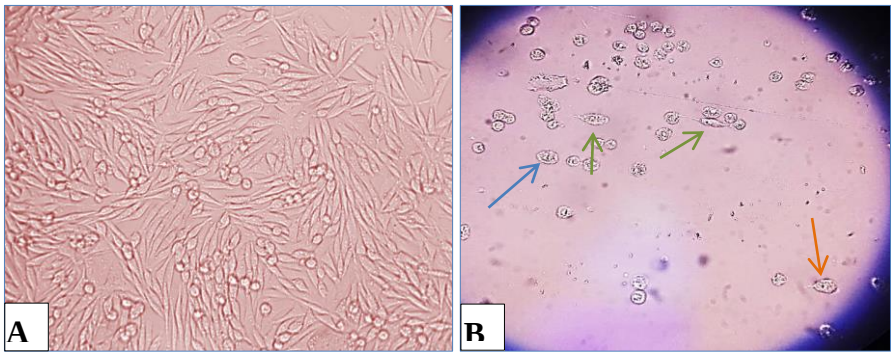

Figure (1): Effect of tested compound (quinine) on the morphologies of RD cells. Images obtained with an inverted phase contrast microscope (200×) after 24 h (A) control A-Normal monolayer confluent RD. (B) exposure of the cells at 60 µg/ml: disruption of monolayer, dependent shrinkage and an elongated appearance, condensed and DNA fragmentation.

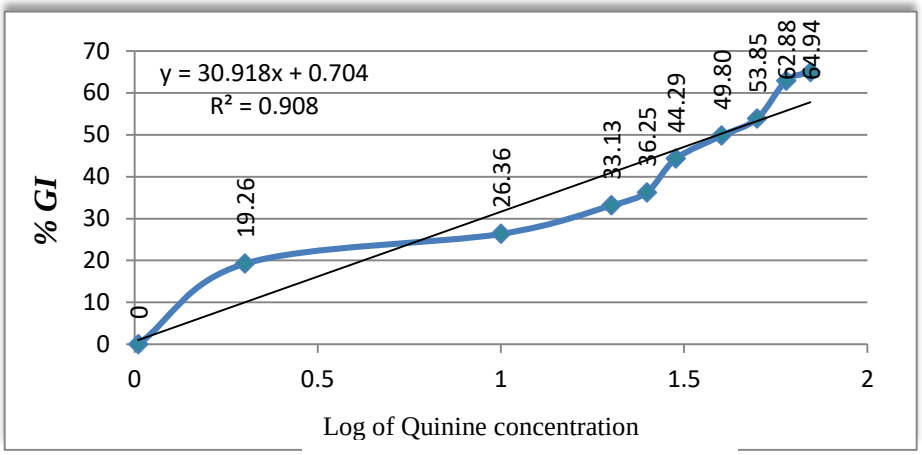

Figure (2): Cytotoxicity of Quinine presented by plotting of drug concentration "log" versus GI% values.

Molecular docking

The findings of the molecular docking experiment (Table 2) indicate that Quinine exhibits different affinities of binding to the major oncogenic proteins, with the strongest interaction being for HSP90 (-8.8 kcal/mol), followed by P-mTOR (-7.5 kcal/mol), Bcl-2 (-7.4 kcal/mol), and Rac1 (-7.1 kcal/mol).

Table (2): Molecular docking score of the four potential targets for quinine.

N	Target	PDB ID	Binding Affinity (kcal/mol)
1	Rac1	3th5	-7.1
2	HSP90	3qdd	-8.8
3	P-mTOR	4jvs	-7.5
4	BCL-2	2w3i	-7.4

Rac1: Ras-related C3 botulinum toxin substrate, HSP90: Heat Shock Protein 90, P-mTOR: Phosphorylated mechanistic Target of Rapamycin, BCL-2: B-cell lymphoma 2.

The 2D interaction diagram provides data regarding the binding mode of Quinine within the Rac1 active site. Quinine forms conventional hydrogen bonds with GLU31 and TYR32 that contribute significantly to binding stability, along with a Pi-Donor Hydrogen Bond interaction that

stabilizes the ligand. Hydrophobic interactions also play an important role as the quinoline moiety engages in π-π T-shaped stacking with TYR32 and alkyl and π-alkyl interactions with LYS16, ALA13, and PHE28 are seen to contribute to stability. Furthermore, van der Waals interactions from residues VAL14, THR17, CYS18, PRO29, and ILE33 contribute weak but significant stabilizing interactions that can maintain Quinine within the binding pocket see figure (3). While figure(4) illustrates the way Quinine interacts with important residues of the HSP90 binding pocket. A standard hydrogen bond with ASN51 is accountable for stabilizing the binding, and other carbon-hydrogen bond interactions provide further stabilization to the ligand. More critical are hydrophobic interactions, with the quinoline ring of Quinine taking part in Pi-Pi stacking interactions with PHE138 and TRP162, which are liable for ligand stabilization in the active site. Additionally, alkyl and Pi-alkyl interactions with residues such as LEU107, MET98, and TYR139 also enhance the binding. Aside from that, weak van der Waals contacts from residues such as ALA55, ASP54, and ALA111 also stabilize Quinine in the binding pocket for a stable interaction. The molecular docking result figure (5) for P-mTOR and Quinine shows strong interaction motifs and binding energies. The ligand interacts with various amino acids by van der Waals forces, hydrogen bonds, pi-pi stacking, and alkyl interactions. Strong hydrogen bonding with VAL2240 contributes to ligand stability. Pi-pi stacking and T-shaped interactions with TYR2225 and TRP2239 indicate aromatic interactions, which are crucial for ligand stabilization in the binding pocket. Besides, hydrophobic interaction with ILE, LEU, and MET enhances the ligand's binding affinity. The 2D interaction plot figure (5) illustrates Quinine interacting with important residues of the BCL-2 binding pocket. Pi-alkyl interactions are observed with LEU96, ALA108, PHE71, TYR67, and MET74, which add to the stabilization of the ligand in the pocket. Van der Waals interactions with PHE63, PHE112, ASP70, and GLU95 are also suggestive of further stabilization. The molecular docking experiment revealed that Quinine exhibited high degrees of interactions with certain major oncogenic proteins involved in the pathophysiology of rhabdomyosarcoma (RMS). Most notably, HSP90 appears to be an extremely worthwhile target for Quinine inhibition. Quinine bound strongly to HSP90 through hydrogen bonding with ASN51 and Pi-Pi stacking interactions with PHE138 and TRP162, as indicated in Figure (4). As HSP90 is an important molecular chaperone that stabilizes numerous oncogenic proteins central to RMS development (25), HSP90 inhibition may disrupt multiple downstream signalling pathways simultaneously. Quinine binds to a variety of proteins including Rac1 (through GLU31 and TYR32), P-mTOR (through VAL2240), and Bcl-2 (through Pi-alkyl and van der Waals interactions). Its binding to HSP90 is particularly significant due to its broad effect on the stability of oncogenic clients that include motility, survival, and proliferation factors. By blocking the activity of HSP90, Quinine might have the potential to destabilize several oncogenic proteins simultaneously, providing a more integrated therapeutic approach rather than targeting single proteins such as Rac1 or mTOR. Therefore, from the results obtained, HSP90 emerges as the most important target for the anti-cancer

effect of quinine, given that its inhibition may trigger the global disruption of oncogenic signalling pathways in RMS. Consequently, HSP90 presents itself as a candidate for further investigation of the multi-target inhibitory action of Quinine in RMS therapy. In RMS, elevated Rac1 levels could be making the tumour cells more aggressive, with a greater capacity to move and invade other regions.Rac1 is a GTPase family member that is present in numerous cells. It plays a significant role in numerous signalling events implicated in cancer (26). Collectively, the results of current study add to the mounting evidence of the anticancer prospects of natural products, particularly plant alkaloids such as quinine, as promising leads for targeted cancer treatments (27-30).

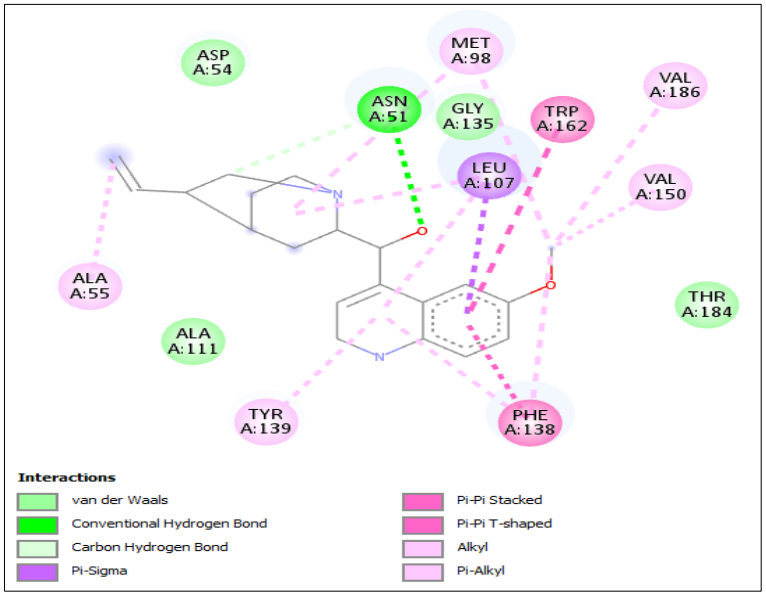

Figure (3): The two-dimensional interaction of Rac1 target protein with Quinine with active site residues.

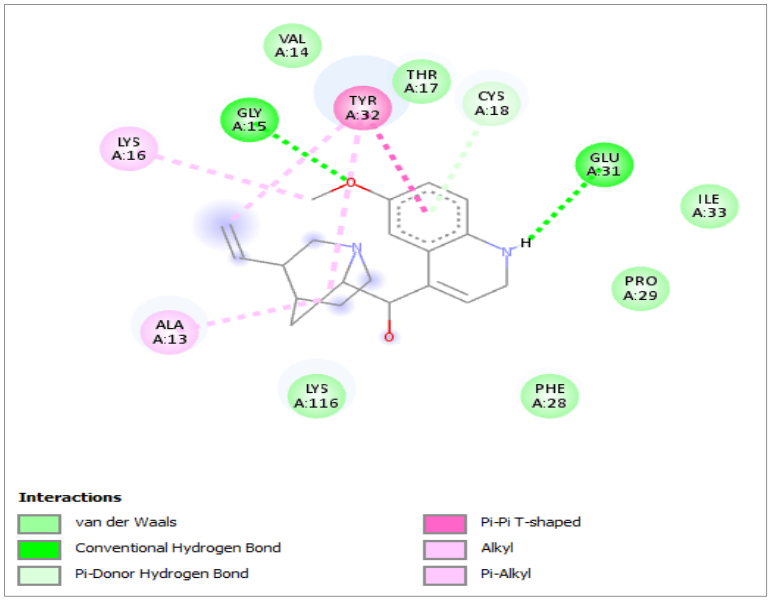

Figure (4): The two-dimensional interaction of HSP90 target protein with Quinine with active site residues.

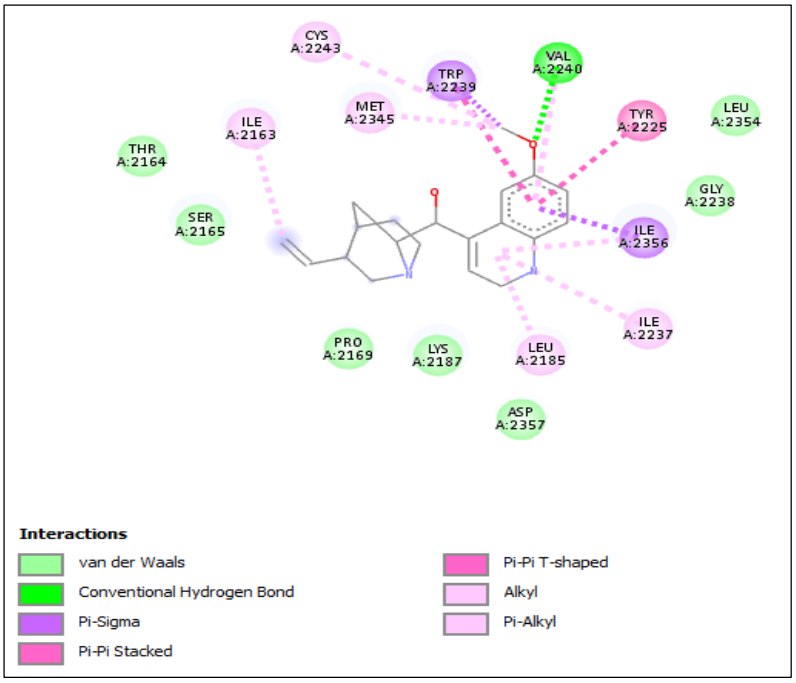

Figure (5): The two-dimensional interaction of p-mTOR target protein with Quinine with active site residues.

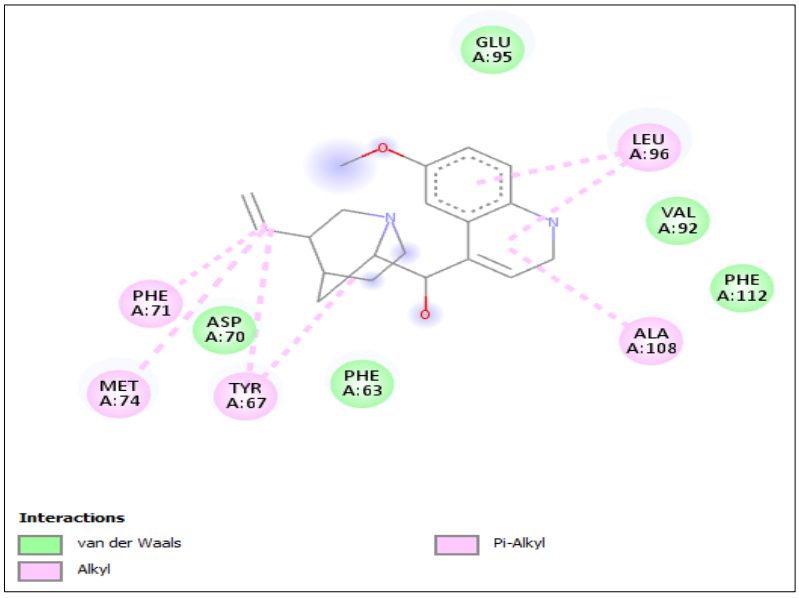

Figure (6): The two-dimensional interaction of BCL-2 target protein with Quinine with active site residues.

Conclusion

Current study shows the therapeutic potential of the natural alkaloid Quinine as an anti-proliferative agent against RD cells in a dose-dependent manner. Its cytotoxic activities are linked with its interaction with the critical oncogenic proteins, particularly HSP90, a protein involved in tumor growth. Molecular docking analysis showed that Quinine can strongly interact with HSP90, thus potentially inhibiting multiple oncogenic pathways simultaneously. In addition, its cross-talks with Rac1, mTOR, and Bcl-2

also support its ability to hinder cancer cell survival and growth. These findings suggest that Quinine could be explored as a lead multi-target drug candidate for RMS with great promise, which warrants further investigation of its mechanism of action and potential in the clinic.

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Ethical Approval

The experimental protocol was approved by the College of Science, University of Kufa, Iraq.

References

1. Norfazlina, M. N.; Zuraina, M. F.; Rajab, N. F.; Nazip, S. M.; Rumiza, A. R.; Zaila, C. S., et al. (2014). Cytotoxicity study of Nigella sativa and Zingiber zerumbet extracts, thymoquinone and zerumbone isolated on human myeloid leukemia (HL60) cell. In The Open Conference Proceedings Journal, 4(2): 99-107.
2. Lu, J. J.; Bao, J. L.; Chen, X. P.; Huang, M. and Wang, Y. T. (2012). Alkaloids isolated from natural herbs as the anticancer agents. Evidence-Based Complementary and Alternative Medicine, 2012(1), 485042.
3. Achan, J.; Talisuna, A. O.; Erhart, A.; Yeka, A.; Tibenderana, J. K.; Baliraine, F. N., et al. (2011). Quinine, an old anti-malarial drug in a modern world: role in the treatment of malaria. Malaria journal, 10, 1-12.
4. Krishnaveni, M.; Suresh, K. and Arunkumar, R. (2016). Antiproliferative and apoptotic effects of quinine in human Hep-2 laryngeal cancer and KB oral cancer cell. Bangladesh Journal of Pharmacology, 11(3), 593-602.
5. Solary, E.; Velay, I.; Chauffert, B.; Bidan, J. M.; Caillot, D., Dumas, M., et al. (1991). Sufficient levels of quinine in the serum circumvent the multidrug resistance of the human leukemic cell line K562/ADM. Cancer, 68(8), 1714-1719.
6. Aderanti, T.; Marshall, J. M. and Thekkiniath, J. (2025). Effect of protease inhibitors on the intraerythrocytic development of Babesia microti and Babesia duncani, the causative agents of human babesiosis. Journal of Eukaryotic Microbiology, e13064.
7. Karlsson, K. K.; Hellgren, U.; Alván, G. and Rombo, L. (1990). Audiometry as a possible indicator of quinine plasma concentration during treatment of malaria. Transactions of the Royal Society of Tropical Medicine and Hygiene, 84(6), 765-767.
8. Kayser, O. (2024). From the Maluku to Molecules: How Natural Substances Write History. Springer Nature.
9. Genne, P.; Duchamp, O.; Solary, E.; Pinard, D.; Belon, J. P.; Dimanche-Boitrel, M. T., et al. (1994). Comparative effects of quinine and cinchonine in reversing multidrug resistance on human leukemic cell line K562/ADM. Leukemia, 8(1), 160-164.
10. Al-Hadad, S. A.; Al-Jadiry, M. F.; Al-Darraji, A. F.; Al-Saeed, R. M.; Al-Badr, S. F. and Ghali, H. H. (2011). Reality of pediatric cancer in Iraq. Journal of pediatric hematology/oncology, 33, S154-S156.
11. Al–Niaimi, A. (2006). Oral malignant lesions in a sample of patients in the north of Iraq (Retrospective study). Al–Rafidain Dental Journal, 6(2), 176-180.
12. Omar, S. K.; Al-Kzayer, L. F. and Mahmood, K. I. (2010). Non CNS pediatric malignancies in Mosul. Annals of the College of Medicine Mosul, 36(1), 86-90.
13. Mahdi, N. K.; Al-Sadoon, M. A. and Hassan, G. K. (2007). Cryptosporidiosis and immunological status in children with malignant diseases. Medical Journal of Basrah University, 25(1), 1-6.
14. Li, C.; Li, Z.; Song, L.; Meng, L.; Xu, G.; Zhang, H., et al. (2021). GEFT inhibits autophagy and apoptosis in rhabdomyosarcoma via activation of the Rac1/ Cdc42-mTOR signaling pathway. Frontiers in Oncology, 11, 656608.
15. Singh, S.; Abu-Zaid, A.; Lin, W.; Low, J.; Abdolvahabi, A.; Jin, H., et al. (2021). 17-DMAG dually inhibits Hsp90 and histone lysine demethylases in alveolar rhabdomyosarcoma. iScience, 24(1).

16. Nikzad, S. and Hashemi, B. (2014). MTT assay instead of the clonogenic assay in measuring the response of cells to ionizing radiation. Journal of Radiobiology, 1(1), 3-8.
17. Alhammer, A. H.; Alkufi, S. G.; Al-Juboori, S. I. and Mudhafar, S. A. (2025). KIF15 inhibitor suppresses the proliferation and migration, and induces the apoptosis of breast cancer cells. World Academy of Sciences Journal, 7, 3.
18. Mohd Shafiee, M. A.; Muhamad Asri, M. and Alwi, S. S. (2021). Review on the in vitro cytotoxicity assessment in accordance to the international organization for standardization (ISO). Malaysian Journal of Medicine and Health Sciences, 17, 261-269.
19. Krishnaveni, M. and Suresh, K. (2015). Induction of apoptosis by Quinine in human laryngeal carcinoma cell line. International Journal of Current Research and Academic Review, 3(3), 169-178.
20. Aziz, D. Z.; Hadi, M. A.; Al-Kelaby, K. K. A.; Abdullah, Z. A.; Hamza, A.; Altaee, A. A., et al. (2023). Cytotoxic and Antioxidant Activity of Linseeds Against Rhabdomyosarcoma Cell Line. Advancements in Life Sciences, 10, 67-72.
21. El Omari, N.; Bakrim, S.; Bakha, M.; Lorenzo, J.M.; Rebezov, M.; Shariati, M.A., et al. (2021). Natural bioactive compounds targeting epigenetic pathways in cancer: a review on alkaloids, terpenoids, quinones, and isothiocyanates. Nutrients, 13(11), 3714.
22. Pagano, P.; Bertoncini, A.; Pagano, A.; Nisa, M. U.; Raynaud, C.; Balestrazzi, A., et al. (2024). Exposure of Arabidopsis thaliana Mutants to Genotoxic Stress Provides New Insights for the Involvement of TDP1α and TDP1β genes in DNA-Damage Response. Plant, Cell and Environment, 47(12), 5483-5497.
23. Vergoten, G. and Bailly, C. (2024). Interaction of norsecurinine-type monomeric and dimeric alkaloids with α-tubulin: A molecular docking study. Exploration of Drug Science, 2(3), 277-291.
24. Byun, M. R.; Kim, S. H.; Woo, R.; Noh, S. J.; Joo, S. H.; Jung, Y. S., et al. (2025). Quinine inhibits myogenic differentiation by disrupting AKT signaling pathway. Toxicological Research, 41(1), 81-90.
25. Ren, X.; Li, T.; Zhang, W. and Yang, X. (2022). Targeting heat-shock protein 90 in cancer: an update on combination therapy. Cells, 11(16), 2556.
26. Wang, Y.; Wang, B.; Li, P.; Zhang, Q. and Liu, P. (2017). Reduced RAC1 activity inhibits cell proliferation and induces apoptosis in neurofibromatosis type 2 (NF2)-associated schwannoma. Neurological Research, 39(12), 1086-1093.
27. Mahmood, H. M.; Mohammed, A. K. and Fleih, M. T. (2016). Cytotoxic effect of pyomelanin pigment produced from local Pseudomonas aeruginosa isolates on different cell lines using MTT assay. Iraqi journal of biotechnology, 15(1).
28. Mohammed, I. H. and Abdullatif, M. H. (2017). Effect of vincristine and vinblastine from Vinca rosa on microtubulues of tumor H22 cell line (hepatic cell line). Iraqi journal of biotechnology, 16(3).
29. Shamran, D. J.; Al-Jumaili, E. F. A. and Tawfeeq, A. T. (2020). Cytotoxicity effect of glucokinin isolated from Bauhinia variegata against several cancer cell lines. Iraqi journal of biotechnology, 19(1).
30. Shaker, L. M.; Al-Amiery, A. A. and Kadhum, A. A. H. (2023). Advances in Drug Delivery Systems: A Mini-Review. Al-Ameed Journal for Medical Research and Health Sciences, 1(1), 3.