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Research Article

PHYTOCHEMICAL CHARACTERIZATION AND ANTICANCER POTENTIAL OF *QUISQUALIS INDICA* L.: AN *IN SILICO* APPROACH

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ABSTRACT

Objectives: The aim is to isolate and identify the bioactive molecules of *Quisqualis indica*, to analyze their chemical profiles and to evaluate their anti-tumor activity by targeting the proteins in question.

Methods: The leaves of *Q. indica* were collected, identified, and extracted with 50% hydroalcohol by means of the Soxhlet method. The extract from the crude oil was fractionated and quisqualic acid isolated by means of silica gel and Sephadex LH-20 chromatography. Chemical profiling was carried out by means of high-performance liquid chromatography-diode array detector-electrospray ionization mass spectrometry (HPLC-DAD-ESI/MS), Fourier transform infrared (FTIR), and proton nuclear magnetic resonance (NMR). Molecular docking of quisqualic acid to tumor-associated proteins (2PIO, epidermal growth factor receptor, human epidermal growth factor receptor 2, vascular endothelial growth factor receptor 2, mammalian target of rapamycin, programmed death-ligand 1) has been performed with the help of the SwissDock and Discovery Studio Visualizer.

Results: The presence of quisqualic acid was confirmed by HPLC-DAD-ESI/MS analysis, as evidenced by its retention time at 5 min, a ultraviolet absorbance maximum at 230 nm, and a characteristic MS fragmentation pattern, including a deprotonated molecular ion $(M–vH)^-$ at m/z 146 and MS^2 fragment ions at m/z 84, 102, and 112. Functional analyses, such as FTIR, and NMR confirm the presence of major functional groups such as hydroxyl groups and aromatic substances. *In silico* docking revealed a moderate-to-high binding affinity for quisqualic acid to cancer-related receptors such as androgen receptor (−6.010 kcal/mole) and VEGFR2 (−5.456 kcal/mole), which implicates quisqualic acid in the treatment of prostate cancer and angiogenesis.

Conclusion: *Q. indica* has an immense anticancer potential, particularly against the target tumors of the prostate and colorectal cancer. Its active ingredient, quisqualic acid, has good binding properties and merits further investigation *in vivo* and in clinical trials.

Keywords: *Quisqualis indica*, High-performance liquid chromatography-diode array detector-elecctrospray ionization mass spectrometry, Fourier transform infrared spectra, Proton nuclear magnetic resonance, Quisqualic acid, anticancer.

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INTRODUCTION

Traditional medicine has been a key component of global health systems for thousands of years and continues to be today. The World Health Organization reports that in some developing countries, nearly 80% of the population relies on traditional medicine to meet basic needs, including chronic conditions such as cancer [1]. Medical systems such as Ayurveda, Siddha, Unani, and Traditional Chinese Medicine are based on herbal medicine, nutrition, and mental health and offer holistic approaches complementary to modern therapies [2-4].

Cancer remains one of the most pressing public health challenges and is the second leading cause of death in the world [5]. Despite advances in diagnosis and treatment, conventional cancer treatments often face barriers such as high toxicity, resistance, and side effects [6]. This has led to renewed interest in integrating traditional medicine into modern oncology. Plant-based therapies, with their multi-target mechanisms, are a promising alternative or complement to synthetic chemotherapeutic agents [7,8].

Originally, medicinal plants were used to prevent and treat tumors. Ancient Ayurvedic texts such as the Charaka Samhita describe conditions such as arbuda (cancer) and detailed herbal remedies that are used to treat inflammation and swelling [9]. Plants have a wide range of phytochemical constituents, such as alkaloids, flavonoids, terpenes, and saponins, which have anti-inflammatory, antioxidant, anti-inflammatory, anti-paraphylactic, and anti-cancer properties [10-13]. For example, population studies show that a high intake of fruits and vegetables is associated with a reduced risk of developing cancer, presumably due to their bioactive ingredients [14].

It is widely used in Ayurvedic, folk, and Chinese traditional medicine for a variety of ailments, including intestinal worms, diarrhea, skin infections, fever, and inflammation [15-17]. Seeds are anthelmintic, while leaves and flowers are used to treat digestive disorders and pain [18].

Plant pharmacology studies with *Quisqualis indica* (*Q. indica*) have identified a number of compounds, including quisqualic acid, rutin, L-proline, L-asparagine, and trigonelline [19,20]. Quisqualic acid is a known agonist of alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid and metabotropic glutamate receptors, both of which are involved in cellular signaling pathways involved in the growth of tumors [21,22]. Molecular docking studies indicate that quisqualic acid is effective in targeting tumors, supporting its potential as a natural anti-cancer agent [23,24].

Moreover, extracts of *Q. indica* were shown *in vitro* to have antioxidant and anti-inflammatory properties consistent with its traditional use in inflammatory and parasitic diseases [25]. Many successful cancer drugs

are derived directly from plants, often inspired by traditional medicines. For example, vincristine from *Catharanthus roseus*, paclitaxel from *Taxus brevifolia*, and camptothecin from *Camptotheca acuminata* are all derived from the ethnomedicine [26,27]. With the growing interest in plant-based therapies worldwide, *Q. indica* is a potential candidate for further research, particularly in the areas of cancer prevention and immunomodulation [28,29].

METHODS

Plant collection and extraction

Fresh *Q. indica* leaves collected from the nearby botanical gardens were gathered, inspected, and carefully dried. The dried plant material was ground into a fine powder and then extracted by the use of the Soxhlet method with a solvent of 50% hydroalcohol. The crude extract was obtained by filtering the extract and concentrating it under lower pressure using a rotary evaporator.

Fractionation and isolation

After dissolution of the crude extract in water, it was subsequently separated by means of hexane, chloroform, and ethyl alcohol. For the silica gel column chromatography of ethyl acetate, which is expected to be rich in flavonoids, including quisqualic acid, a gradient solvent system consisting of chloroform: methanol (95:5) with increasing polarity was used. After the thin-layer chromatography (TLC) analysis with ethyl acetate: methanol:water (80:10:10) as solvent system, the fractions showing ultraviolet (UV)-active spots with a retention factor value comparable to quisqualic acid were pooled together. For further purification, the methanol used as an eluent in Sephadex LH-20 column chromatography.

Analytical techniques

Silica gel plates 60 F254 were used for the TLC and for the high-performance liquid chromatography (HPLC) analysis of the compounds. The solvent was removed by means of a rotary evaporator, and the flavonoids were determined by UV irradiation. Quisqualic acid was the reference standard. The chemical composition of the extract was examined using HPLC and a 230 nm UV detector. Quisqualic acid was the focus of the retention time (RT) and UV absorption spectra for the molecular identification. By examining the characteristic absorption peaks, functional groups of the extract have been determined using the Fourier transform infrared (FTIR) spectra. Chemical shifts and functional groups are determined by proton nuclear magnetic resonance (^{1}H NMR) spectroscopy [30-32].

In silico screening

The docking study was carried out using visualization tools and a website. The following hardware and software were used in the study: hardware configuration: Dell notebook PC, processor Intel (R) Pentium (R) processor 4415U at 2.30 GHz, memory 4.00 GB (3.87 GB usable), operating system Windows 10 (64-bit), version 22H2, build 19045.5371.

Software and online tools: SwissDock (https://www.swissdock.ch/index.php) used to calculate molecular docking. Visualization of protein preparation and docking has been done using Discovery Studio Visualizer (DS Visualizer). Use the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) to get the structure in SMILES format. Use the Protein Data Bank (PDB) (https://www.rcsb.org/) to retrieve receptor structures in PDB format. The SwissDock (based on AutoDock Vina) was used in molecular docking studies to determine the affinity of the target protein to the ligand. The workflow consisted of the following steps: first, obtaining the SMILES format for the ligand from PubChem. The structure of the ligand was prepared and converted to PDB format using DS Visualizer. Second, protein structures have been extracted from the PDB collection. Water molecules and non-essential heteroatoms are eliminated. Third, the binding site was determined either from literature or by means of a catalytic liquid suspension. DS Visualizer was used to define the grid of desks around the active server. Fourth, purified ligand and protein were recorded in SwissDock. For a focused docking approach with default parameters, the XYZ coordinate points of the ligands are specified. Flexible ligand docking is performed using default docking parameters. The fifth and final step is to analyze the docked pose for binding affinity (ΔG in kcal per mole). The lowest free energy and hydrogen bond interactions of the best binding conformation were selected. The DS Visualizer was used to visualize and analyze the interaction [33,34].

RESULTS

Collection and authentication of plant material

Plants were collected from the local area of Varanasi. Professor N. K. Dubey of Banaras Hindu University in Varanasi verified the authenticity of the plants. For *Q. indica*, the voucher specimen number is Combret. 2022/1.

HPLC-diode array detector-electrospray ionization mass spectrometry (HPLC-DAD-ESI/MS)

High-performance liquid chromatography of Q. indica was performed using detection at 230 nm to separate and identify bioactive compounds in a 50% hydroalcoholic extract. The chromatogram showed a prominent peak at a RT of 5 min, indicating the presence of a compound absorbing strongly at this wavelength (Fig. 1 and 2, Table 1).

This compound was further analyzed by HPLC-DAD-ESI/MS, where the maximum UV absorbance (λ_{max}) was also found at 230 nm, consistent with quisqualic acid. The molecular ion peak in negative ion mode appeared at m/z 146 ([M−vH]$^-$), and MS^2 fragmentation produced ions

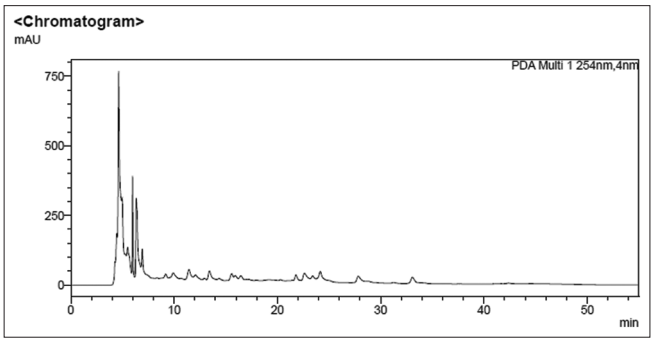


Fig. 1: Representative high-performance liquid chromatography chromatogram of *Q. indica* 50% hydroalcoholic extract detected at 230 nm. A prominent peak at an RT of 5 min indicates the presence of a major bioactive compound with strong absorbance at this wavelength

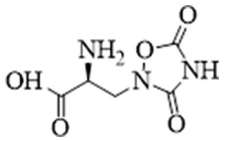


Fig. 2: Chemical structure of quisqualic acid, a bioactive amino acid with an oxazolidine-2,4-dione ring, identified as a major compound in *Q. indica*

Table 1: Tentative identification of the major compound by the HPLC-DAD-ESI/MS analysis of the 50% hydroalcoholic extract of *Quisqualis indica.*

Peak	Rt (min)	λ_{max} (nm)	(M-vH)$^-$ (m/z)	MS^2 (m/z)	Tentative Identification
1	5	230	146	84, 102, 112	Quisqualic Acid

at m/z 84, 102, and 112. These spectral features support the tentative identification of the compound as quisqualic acid. Overall, this analytical method successfully revealed the presence of quisqualic acid in the plant extract, contributing valuable information to the phytochemical profile and potential medicinal relevance of Q. indica.

FTIR spectroscopy

FTIR spectroscopy identified key functional groups in *Q. indica*. The absorption peaks observed were 1111.29 cm^{-1} (C-O stretching in alcohols, ethers, esters), 1384.12 cm^{-1} (C-H bending in methyl groups), 1609.33 cm^{-1} (N-H bending, C=C stretching in alkenes/aromatic rings), and 3381.81 cm^{-1} (O-H stretching in alcohols/phenols). These indicate the presence of alkanes, alcohols, esters, amines, and aromatic compounds, contributing to its chemical and therapeutic properties Fig. 3.

Nuclear magnetic resonance (NMR) spectroscopy

^{1}H NMR spectroscopy revealed key chemical shifts in *Q. indica*. 0.01–1.32 ppm (CH_2, methylene groups), 2.12–2.34 ppm (CH_3, methyl groups), 1.82–3.37 ppm (Ar-H, aromatic protons), 3.33–4.12 ppm (-CH-NH_2, methane protein, OH, hydroxyl groups), and 4.96–5.14 ppm (CH_3, methyl groups in side chains). These signals indicate the presence of aliphatic chains, aromatic compounds, and hydroxyl functional groups Fig. 4.

***In silico* screening**

This study looked at how quisqualic acid attaches to different proteins in the body (Table 2), including those involved in lung cancer and other proteins that are involved in other types of cancer. The docking results provide an idea of binding affinity, stability, and therapeutic potential of the ligand.

Binding affinity and interaction analysis

The docking study focused on lung cancer-related receptors such as epidermal growth factor receptor (EGFR) (1M17, 6JXT) and programmed death-ligand 1 (PD-L1) (5X8L), as well as on other targets such as vascular endothelial growth factor receptor 2 (VEGFR2) (4ASD), mammalian target of rapamycin (mTOR) (4JT6), androgen receptor (2PIO), and human epidermal growth factor receptor 2 (HER2) (3PP0). The following summary of the docking scores and the hydrogen bond interactions is valuable.

Lung cancer receptor analysis

The interaction with EGFR (1M17 and 6JXT) from the docking simulation showed that quisqualic acid has a moderate binding affinity to it with a docking score of −5.168 (1M17) and −5.961 (6JXT). The ligand has multiple hydrogen bonds, which indicates a reasonable stability, but the length of the bonds (>2.5Å) suggests that the interaction is weak compared to other targets such as the androgen receptor. Due to the importance of EGFR in non-small cell lung cancer, the lowest binding affinity was −4.994 indicating that quisqualic acid has some inhibitory potential but may need further refinement to increase its binding affinity and selectivity. Although there were six observed hydrogen bonds, their length indicates greater instability than stability, which could render the ligand ineffective as an immunosuppressant. This suggests that quisqualic acid may not be the optimal inhibitor of PD-L1, and therefore, a more neutral

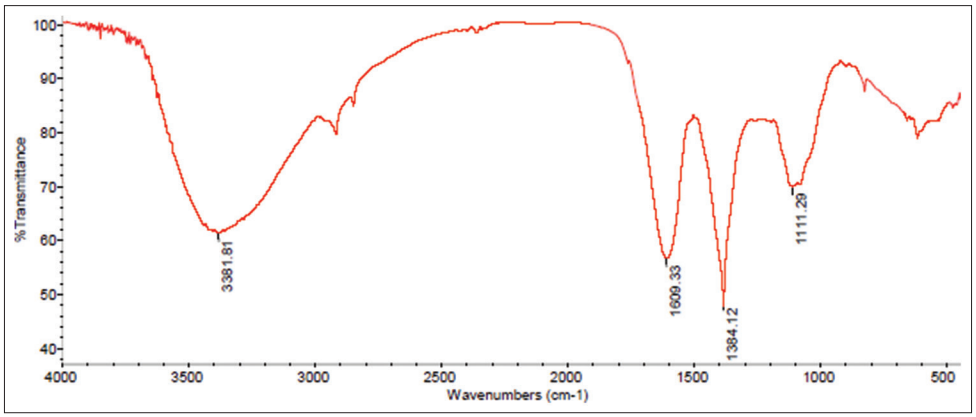


Fig. 3: Fourier transform infrared spectrum of *Q. indica* showing peaks at 1111.29, 1384.12, 1609.33, and 3381.81 cm^{-1}, indicating alcohols, esters, amines, alkanes, and aromatic compounds.

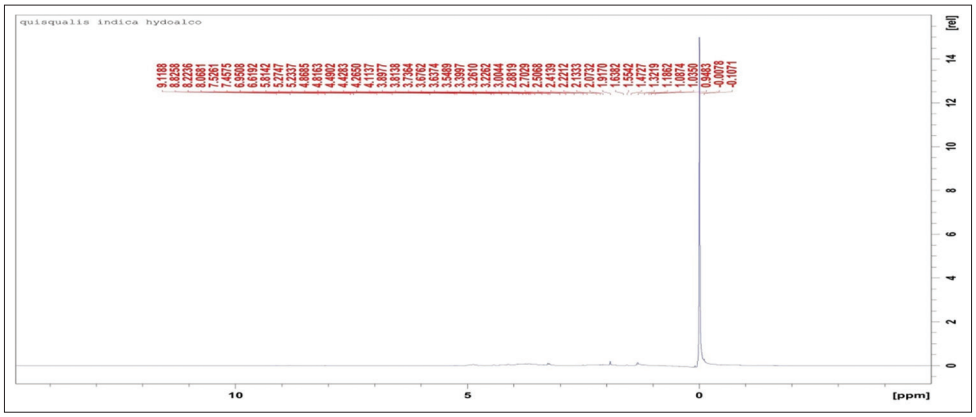
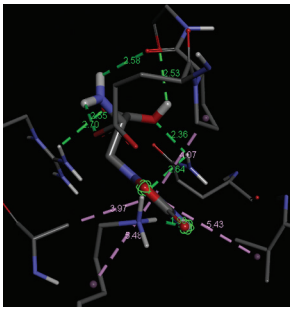
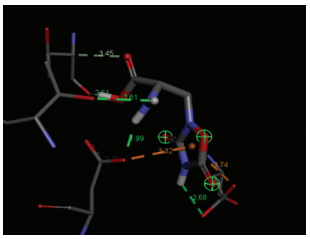
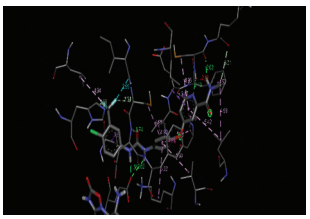
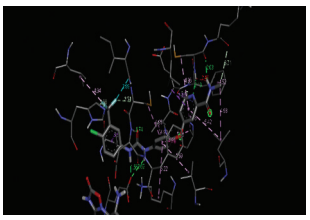
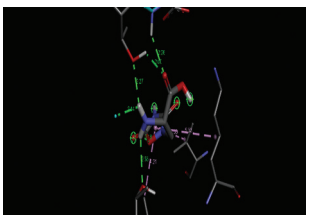
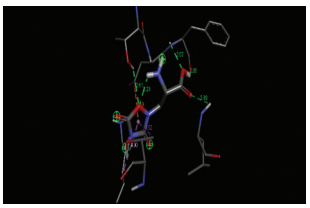
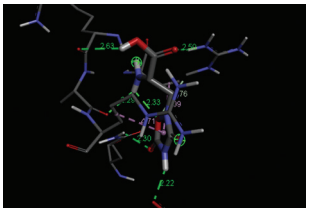


Fig. 4: Proton nuclear magnetic resonance spectrum of *Q. indica* showing key shifts indicating methylene (0.01–1.32 ppm), methyl (2.12–2.34 ppm, 4.96–5.14 ppm), aromatic protons (1.82–3.37 ppm), and hydroxyl/amine groups (3.33–4.12 ppm), suggesting aliphatic, aromatic, and hydroxyl-containing compounds.

Table 2: Docking results of *Q. indica* compound with cancer-related receptors: receptor coordinates, ligand-receptor hydrogen bond interactions (with bond lengths), and docking scores against various cancer targets.

Type of Cancer	Receptor	Coordinates (XYZ)	Ligand-receptor interaction	Conventional hydrogen bond	Docking score
Prostate Cancer	Androgen receptor (2PIO)	53.267463 7.240293 13.709927		7 (1.93Å, 2.36Å, 2.53Å, 2.55Å, 2.58Å, 2.64Å and 2.70Å)	−6.010
Pancreatic Cancer	mTOR (4JT6)	16.884115-16.687231-51.886327		4 (1.99Å, 2.61Å, 2.61Å and 2.68Å)	−4.453
Colorectal Cancer	VEGFR2 (4ASD)	-30.002000-0.306000-9.367000		5 (1.56Å, 1.74Å, 2.03Å, 2.10Å and 2.62Å)	−5.456
Breast Cancer	HER2 (3PP0)	25.856397 30.612118 7.552074		6 (1.92Å, 2.27Å, 2.37Å, 2.72Å, 2.85Å and 2.85Å)	−5.628
Lung Cancer	EGFR (1M17)	22.013690 0.252828 52.794034		6 (2.00Å, 2.14Å, 2.18Å, 2.26Å, 2.27Å and 2.53Å)	−5.168
Lung Cancer	EGFR (6JXT)	-15.553270 53.427757 7.660757		5 (2.09Å, 2.23Å, 2.52Å, 2.61Å and 2.89Å)	−5.961
Lung Cancer	PD-L1 (5X8L)	28.572626 17.966452 63.240140		6 (2.20Å, 2.29Å, 2.30Å, 2.33Å, 2.50Å and 2.63Å)	−4.994

EGFR: Epidermal growth factor receptor, HER2: Human epidermal growth factor receptor 2, VEGFR2: Vascular endothelial growth factor receptor 2, mTOR: Mammalian target of rapamycin, PD-L1: Programmed death-ligand 1

modification or different formulation of the ligands is required to improve the interaction with the target.

Molecular docking of the ligand with cancer-targeting receptors demonstrated the highest binding affinity toward the androgen receptor (2PIO) in prostate cancer with a docking score of −6.010 and seven hydrogen bonds (1.93–2.70 Å). Other significant interactions were EGFR (6JXT) in lung cancer (−5.961, five H-bonds), HER2 (3PP0) in breast cancer (−5.628, six H-bonds), VEGFR2 (4ASD) in colorectal cancer (−5.456, five H-bonds), EGFR (1M17) in lung cancer (−5.168, six H-bonds), mTOR (4JT6) in pancreatic cancer (−4.453, four H-bonds), and PD-L1 (5X8L) in lung cancer (−4.994, six H-bonds). These findings demonstrate high ligand interactions with various targets of cancer, namely prostate and lung cancer receptors.

DISCUSSION

This study confirms the presence of quisqualic acid in *Q. indica* using HPLC-DAD-ESI/MS, supported by FTIR and ^{1}H NMR data indicating key functional groups such as hydroxyl, methyl, and aromatic compounds. These findings highlight the phytochemical richness of the 50% hydroalcoholic extract.

In silico docking showed strong binding of quisqualic acid to multiple cancer-related receptors. The highest affinity was observed with the androgen receptor (2PIO) in prostate cancer (docking score: −6.010, seven hydrogen bonds). Significant interactions were also seen with EGFR (6JXT) in lung cancer (−5.961) and HER2 in breast cancer (−5.628), suggesting broader anticancer potential.

However, weaker binding to PD-L1 indicates limited immunosuppressive potential. Overall, quisqualic acid shows promise, especially against prostate and lung cancer targets, but further biological validation and structural refinement are needed for therapeutic development.

CONCLUSION

Q. indica, traditionally used in various Asian medical systems, has been used for centuries to treat parasitic infections, diarrhea, inflammation, and skin ailments. Its extensive ethnomedicine use indicates a pharmacologically active profile, notably the presence of bioactive phytochemicals that can modulate key biological targets. The aim of this study was to bridge traditional knowledge with modern analytical techniques to assess the plant phytochemical composition and potential anticancer activity, with particular emphasis on quisqualic acid isolation and characterization.

Phytochemical profiling by HPLC-DAD-ESI/MS has allowed for the accurate determination of quisqualic acid with an RT of 2.86 min and a molecular ion peak of 146. The presence of conjugated functional groups typical of glutamate analogues was further supported by the UV absorption at 210-220 nm. Functional groups such as hydroxy (O)-H, amine (N-H), carbonyl (C=O), and carboxyl (C-O) are confirmed by FTIR analysis and are consistent with the expected structure of quisqualic acid. NMR spectroscopy provided further structural confirmation, with NMR signals of the aliphatic and amide proton environment indicating a deshielded carbonyl and methylene moiety, which are consistent with the carboxylic acid moieties of quisqualic acid.

The bioactivity of the compound was evaluated by docking to androgen receptor with significant binding affinity to androgen receptors (docking score: −6.010), VEGFR2 (score: −5.456), EGFR, HER2, and PD-L1. These interactions suggest possible mechanisms by which quisqualic acid can have an anticancer effect, in particular on prostate, breast and lung cancer.

In summary, the study provides both ethnopharmacological validation and scientific evidence of the anticancer potential of *Q. indica*, in particular through the bioactive ingredient quisqualic acid. Integrating modern analytical techniques with traditional knowledge provides a solid basis for further developing this plant as a natural cancer treatment. Future work should focus on bioactivity isolation, mechanistic studies, and preclinical evaluation to fully investigate the therapeutic potential of this medicinal product. Clear inclusion and exclusion criteria have been used to ensure reproducibility and to promote the integration of traditional knowledge with modern scientific verification.

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CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation.

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