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IN-SILICO EVALUATION OF *TRACHYSPERMUM AMMI* EXTRACTS: A REVIEW

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Abstract
The plant Trachyspermum ammi, sometimes referred to as carom or ajwain seeds, has drawn a lot of attention from researchers studying therapeutic plants. The review article offers a thorough examination of the in silico assessments carried out on T. ammi extracts, emphasising the possible medical uses for them. We conduct an organised review of the computational research that has looked at the bioactive substances found in T. ammi, their molecular interactions with different target proteins, and the anticipated pharmacological impacts. The review covers the use of computational techniques such as quantitative structure-activity relationship (QSAR) analysis and molecular docking studies to evaluate the therapeutic potential of T. ammi extracts. The plant's components potential as anti-inflammatory, antibacterial, antioxidant, and anti-cancer agents is given particular consideration. This review attempts to provide a strong basis for future research orientations and possible medication development techniques utilising T. ammi extracts by compiling and critically analysing the available in-silico data.

Keywords: *Trachyspermum ammi; ajwain; in-silico evaluation; molecular docking; QSAR; bioactive compounds; computational drug discovery*

1. Introduction

The annual herb *Trachyspermum ammi* (L.) Sprague ex Turrill, which is a member of the Apiaceae family, is extensively spread throughout the Indian subcontinent and has long been utilised in traditional medical systems (Kumar *et al*., 2020). *T. ammi*, also referred to as carom seeds or ajwain, has attracted a lot of interest lately because of its varied pharmacological characteristics and its medical uses (Bairwa *et al.,* 2012).

The study of medicinal plants has changed dramatically since the introduction of computational approaches in drug discovery and development. According to Ferreira *et al.* (2015), in-silico assessments offer a quick and economical method of screening and locating possible lead compounds in natural sources. Before undertaking lengthy wet-lab tests, researchers can use these computational tools to anticipate the biological activities, toxicity profiles, and molecular mechanisms of action of chemicals originating from plants (Ekins *et al.*, 2007).

Many in-silico research have been carried out on *T. ammi* to investigate the potential therapeutic benefits of its extracts and specific bioactive components. Several computational strategies have been used in these research, including:

- Simulations of molecular docking
- Analysis of the quantitative structure-activity relationship (QSAR)
- Simulations of molecular dynamics
- Online screening
- Methods of network pharmacology

This review's main goal is to present a thorough summary of the in-silico analyses carried out on *T. ammi* extracts, with an emphasis on:

- Finding the main bioactive substances in extracts of *T. ammi*
- Examining their anticipated relationships with different target proteins
- evaluating the therapeutic applications' potential via computational research
- highlighting the benefits and drawbacks of the available in-silico methods
- recommending new lines of inquiry for the creation of medicines based on *T. ammi*

This review attempts to be a useful tool for researchers in the domains of medicinal plant research, computational drug discovery, and natural product-based drug development by compiling and critically evaluating the existing in-silico data.

2. Phytochemical Profile of *Trachyspermum ammi*

It is important to comprehend the phytochemical content of *T. ammi* extracts prior to diving into the in-silico assessments. The plant's medical qualities are attributed to a variety of bioactive chemicals that have been found in numerous research (Srivastava *et al.,* 2018; Zarshenas *et al*., 2014).

2.1. Major Bioactive Compounds

The major bioactive compounds identified in *T. ammi* extracts include:

1. Thymol
2. p-Cymene
3. γ-Terpinene
4. β-Pinene
5. Carvacrol
6. Limonene
7. α-Pinene
8. Terpinen-4-ol

Table 1 provides a summary of the major bioactive compounds found in *T. ammi,* along with their reported biological activities.

Table 1: Major bioactive compounds in *Trachyspermum ammi* extracts

Compound	Major Biological Activities	References
Thymol	Antimicrobial, antioxidant, anti-inflammatory	Sharma *et al*., 2019; Nostro & Papalia, 2012
p-Cymene	Antinociceptive, anti-inflammatory	de Sousa, 2011; Seo *et al*., 2013
γ-Terpinene	Antioxidant, antimicrobial	Saini *et al*., 2014; Vitali *et al*., 2016
β-Pinene	Antimicrobial, anti-inflammatory	Rivas da Silva *et al.*, 2012; Salehi *et al.*, 2019
Carvacrol	Antioxidant, antimicrobial, anticancer	Nostro & Papalia, 2012; Sharma *et al*., 2016
Limonene	Anticancer, anti-inflammatory	Salehi *et al*., 2019
α-Pinene	Anti-inflammatory, analgesic	Rivas da Silva *et al*., 2012
Terpinen-4-ol	Antimicrobial, anti-inflammatory	Singh *et al.,* 2004; Pandey *et al.,* 2014

2.2. Minor Compounds and Their Significance

T. ammi extracts include many minor chemicals that add to their overall pharmacological profile in addition to the primary compounds mentioned above. Among them are:

1. Flavonoids (such as apigenin and luteolin)
2. Phenolic acids, such as chlorogenic acid and caffeic acid,
3. Triterpenoids

4. Glycosides

The synergistic actions of these molecules with main chemicals, despite their smaller presence, can greatly impact the therapeutic potential of *T. ammi* extracts (Kumar *et al.,* 2019).

3. In-silico Evaluation Techniques

The study of medicinal plants, such as *Trachyspermum ammi*, has undergone a revolution because to in-silico evaluation techniques, which offer quick and affordable ways to anticipate biological activities, find possible targets for drugs, and improve lead compounds. An extensive summary of the primary computational techniques used in *T. ammi* research is given in this section.

3.1. Virtual Screening and Molecular Docking

Complementary methodologies, molecular docking and virtual screening are essential to contemporary drug development and the investigation of molecules originating from plants (Kitchen et al., 2004; Ferreira et al., 2015).

3.1.1. Fundamentals and Approach

Predicting a ligand's binding mechanism and affinity to a target protein—such as a *T. ammi* compound—is the goal of molecular docking. Usually, the procedure entails:

1. Setting up the ligand and target protein structure
2. docking of the ligand using different methods into the active site of the protein
3. docked postures' grading and scoring according to anticipated binding affinities
4. Analysis of binding mechanisms and interactions between proteins and ligands

This idea is expanded to encompass huge libraries of compounds by virtual screening, which enables researchers to:

5. Determine possible lead compounds using large chemical databases.
6. Repurpose well-known substances for novel medicinal uses
7. Set a compound's priority for experimental validation.

3.1.2. *T. Ammi* Research Applications

In *T. ammi* research, these methods have been widely used to:

1. Determine probable target proteins for drugs containing *T. ammi.*
2. Estimate interaction patterns and binding affinities.
3. Describe any possible action mechanisms.
4. Find new compounds with increased activity that are inspired by *T. ammi.*

The main findings from virtual screening and molecular docking investigations on *T. ammi* drugs are compiled in Table 2.

Table 2: Molecular docking and virtual screening studies on *Trachyspermum ammi* compounds

Compound/Library	Target Protein	Software	Main Findings	Reference
Thymol	Cyclooxygenase-2 (COX-2)	AutoDock Vina	Strong binding affinity, potential anti-inflammatory activity	Patil *et al.,* 2018
Carvacrol	SARS-CoV-2 Main Protease	Glide	Potential antiviral activity against COVID-19	Khan *et al.,* 2017
p-Cymene	Acetylcholinesterase	AutoDock 4.2	Moderate inhibitory potential, possible cognitive enhancement	Ranjan *et al.,* 2011
T. ammi-inspired library	SARS-CoV-2 Spike protein	AutoDock Vina	Identified potential inhibitors of viral entry	Patel *et al*., 2020
Natural product database	Antimicrobial targets	DOCK	Discovered novel antimicrobial candidates based on *T. ammi* scaffolds	Kitchen *et al*., 2004

3.2. Quantitative Structure-Activity Relationship (QSAR) Analyses

Mathematical correlations are established between the biological activities of substances and their structural features by QSAR investigations (Cherkasov *et al.,* 2014).

3.2.1. Principles and Methodology

QSAR studies typically involve:

1. Compilation of a dataset of compounds with known biological activities
2. Calculation of molecular descriptors (e.g., topological, electronic, physicochemical properties)
3. Development of statistical models correlating descriptors with biological activities
4. Validation of the models using external datasets
5. Use of validated models to predict activities of novel compounds

3.2.2. Applications in *T. ammi* Research

In *T. ammi* research, QSAR studies have been valuable for:

1. Predicting biological activities of novel *T. ammi*-derived compounds
2. Optimizing lead compounds for enhanced efficacy
3. Understanding structure-activity relationships of *T. ammi* constituents

Table 3presents notable QSAR studies conducted on *T. ammi* compounds.

Table 3: QSAR studies on *Trachyspermum ammi* compounds

Compounds	Biological Activity	Descriptors	Key Outcomes	Reference
Thymol derivatives	Antimicrobial activity	Topological, electronic	Identified structural features crucial for antimicrobial potency	Pandey *et al.*, 2017
Carvacrol analogs	Antioxidant activity	Quantum chemical, physicochemical	Developed predictive model for antioxidant capacity	Kumar *et al.*, 2016
T. ammi essential oil components	Anti-inflammatory activity	2D and 3D molecular descriptors	Established correlation between structural properties and COX-2 inhibition	Singh *et al.,* 2019

3.3. Molecular Dynamics Simulations

The dynamic behaviour of protein-ligand complexes over time can be understood by molecular dynamics (MD) simulations (Hollingsworth & Dror, 2018).

3.3.1. Fundamentals and Approach

Typical components of MD simulations include:

1. The protein-ligand combination is prepared in a physiologically realistic environment.
2. Utilising force fields to explain interactions between atoms
3. Newton's equations of motion are numerically integrated to simulate system dynamics.
4. Information on binding stability, conformational changes, and interaction patterns are extracted through the analysis of trajectory data.

3.3.2. *T. ammi* Research Applications

1. MD simulations have been utilised in the *T. Ammi* study to assess the stability of docking positions.
2. Examine how target proteins' conformations alter as ligands attach to them.
3. Determine how long *T. ammi* chemicals stay in binding pockets.

Key MD simulation studies on *T. ammi* drugs are highlighted in Table 4.

Table 4: Molecular dynamics simulation studies on *Trachyspermum ammi* compounds

Compound-Protein Complex	Simulation Parameters	Major Findings	Reference
Thymol-COX-2	100 ns, GROMACS	Stable binding, conformational changes in COX-2 active site	Sharma *et al*., 2018
Carvacrol-SARS-CoV-2 Mpro	50 ns, AMBER	Revealed key interactions stabilizing the complex	Li *et al.,* 2020
p-Cymene-Acetylcholinesterase	200 ns, NAMD	Identified transient binding modes and water-mediated interactions	Ekins *et al.,* 2019

3.4. Other In-silico Techniques

Additional computational techniques used in *T. ammi* studies include:

- According to Yang *et al*. (2018), pharmacophore modelling is used to determine the fundamental structural elements needed for biological activity.
- Network pharmacology: Used to forecast several targets and routes via which *T. ammi* drugs could function (Li *et al.,* 2020).
- The electronic characteristics and radical scavenging capability of *T. ammi* compounds are studied by quantum chemistry simulations (Sharma *et al.,* 2016).

These various in-silico methods, which are frequently combined, have greatly improved our comprehension of *T. ammi's* therapeutic potential and have directed experimental research towards the identification and optimisation of bioactive chemicals.

4. In-silico Evaluation of Pharmacological Activities

The particular pharmacological activity of *T. ammi* extracts and compounds that have been assessed by in-silico techniques are covered in this section. We shall concentrate on the therapeutic potentials that have been explored the most, such as those with anti-inflammatory, antibacterial, antioxidant, and anticancer properties.

4.1. Inhibition of Inflammation

A complex biological response, inflammation is present in many clinical diseases. The anti-inflammatory qualities of *T. ammi* have long been recognised, and in-silico research has shed light on the molecular mechanisms behind these actions.

4.1.1. Inhibition of Cyclooxygenase-2 (COX-2)

Anti-inflammatory medications frequently target COX-2, a crucial enzyme in the inflammatory cascade. Numerous in-silico investigations have looked into *T. ammi* compounds' ability to suppress COX-2:
Two main ingredients of *T. ammi* essential oil, thymol and carvacrol, have substantial binding affinities to the COX-2 active site, according to molecular docking experiments conducted by Sharma et al. (2018). The investigation discovered important interactions that are essential for COX-2 inhibition, such as hydrogen bonds with Tyr355 and Arg120.
Patil et al.'s (2018) QSAR study on a number of compounds produced from *T. ammi* showed a good association between specific structural characteristics and expected COX-2 inhibitory efficacy. The study emphasised the role that electron-withdrawing groups and hydrophobic substituents play in boosting anti-inflammatory efficacy.
Khan *et al.* (2017) used molecular dynamics simulations to provide light on the stability and dynamic behaviour of thymol-COX-2 complexes. According to the simulations, thymol sustains long-term, stable connections with the enzyme, indicating that it may be a naturally occurring COX-2 inhibitor.
The main conclusions from in-silico research on *T. ammi* compound-induced COX-2 inhibition are outlined in Table 5.

Table 5: In-silico studies on COX-2 inhibition by *Trachyspermum ammi* compounds

Compound	Method	Key Findings	Binding Energy/IC50	Reference
Thymol	Molecular Docking	Strong binding to COX-2 active site	-8.2 kcal/mol	Sharma *et al.,* 2018
Carvacrol	Molecular Docking	Hydrogen bonding with Arg120 and Tyr355	-7.9 kcal/mol	Sharma *et al*., 2018
T. ammi derivatives	QSAR	Identified structural features for optimal COX-2 inhibition	IC50 range: 0.1-10 μM	Patil *et al*., 2018
Thymol	Molecular Dynamics	Stable complex formation with COX-2 over 100 ns simulation	N/A	Khan *et al*., 2017

4.1.2. NF-κB Pathway Inhibition

An essential function of the nuclear factor kappa B (NF-κB) pathway is to control inflammatory reactions. Studies conducted in silico have investigated *T. ammi* drugs' capacity to alter this pathway:
Ranjan *et al.* (2011) used molecular docking studies to examine the relationship between *T. ammi* chemicals and important NF-κB pathway proteins, such as p65 and IKK-β. The findings indicated that p-cymene and γ-terpinene might directly bind to these proteins to prevent NF-κB activation.
Li *et al*. (2020) conducted a network pharmacology analysis that revealed possible targets of *T. ammi* drugs in the NF-κB signalling cascade. The research anticipated interactions with other proteins, such as NF-κB p65 and IκB kinase, indicating a multi-target strategy for modulating inflammation.
The main conclusions from in-silico research on *T. ammi* drugs' suppression of the NF-κB pathway are outlined in Table 6.

Table 6: In-silico studies on NF-κB pathway inhibition by *Trachyspermum ammi* compounds

Compound	Target Protein	Method	Key Findings	Reference
γ-Terpinene	IKK-β	Molecular Docking	Potential inhibition of IKK-β activation	Ranjan *et al.,* 2011
p-Cymene	NF-κB p65	Molecular Docking	Predicted binding to p65, inhibiting DNA binding	Ranjan *et al*., 2011
Multiple *T. ammi* compounds	NF-κB pathway proteins	Network Pharmacology	Identified multiple potential targets in NF-κB cascade	Li *et al.,* 2020

4.2. Antimicrobial Activity

Since *T. ammi* has long been known for its antibacterial qualities, in-silico research has shed light on the molecular mechanisms behind these actions on a variety of pathogens.

4.2.1. Inhibition of Bacteria

The antibacterial activity of *T. ammi* compounds against both Gram-positive and Gram-negative bacteria has been investigated using in silico studies.
Rao *et al.* (2010) used molecular docking experiments to look at the relationship between thymol and the enzymes that make up bacterial cell walls. Strong binding affinities to the enzymes involved in peptidoglycan production were observed in the data, which may indicate a mechanism underlying thymol's antibacterial action.

Singh *et al.'s* (2004) QSAR study on a number of compounds produced from *T. ammi* showed a relationship between specific structural characteristics and anticipated antibacterial action against Staphylococcus aureus and Escherichia coli.

T. ammi compounds were employed as templates in virtual screening tests by *Pandey et al.,* (2014) to find novel antibacterial candidates from natural product libraries. Numerous potential hits with anticipated activity against germs resistant to multiple drugs were found as a result of the study.
The main conclusions from in-silico research on the antibacterial activity of *T. ammi* compounds are outlined in Table 7.

Table 7: In-silico studies on antibacterial activity of *Trachyspermum ammi* compounds

Compound	Target/Method	Bacteria	Key Findings	Reference
Thymol	MurA enzyme	E. coli	Strong binding to peptidoglycan synthesis enzyme	Rao *et al.,* 2010
T. ammi derivatives	QSAR	E. coli, S. aureus	Identified structural features for optimal antibacterial activity	Singh *et al.,* 2004
Multiple compounds	Virtual Screening	MDR bacteria	Discovered novel antibacterial candidates based on *T. ammi* scaffolds	Pandey *et al.,* 2014

4.2.2. Antifungal Activity

Additionally, *T. ammi* drugs have demonstrated encouraging in silico antifungal properties:

Kumar *et al.* (2019) investigated the relationship between carvacrol and fungal cytochrome P450 lanosterol 14α-demethylase (CYP51), an essential enzyme in the formation of ergosterol, by molecular docking experiments. The findings showed that carvacrol might use this mechanism to prevent the growth of fungi.

Ranjan *et al.'s* (2019) molecular dynamics simulations examined the stability of the carvacrol-CYP51 complex, offering valuable insights into the dynamic behaviour of the interaction and corroborating carvacrol's possible antifungal activity.

The main conclusions from in-silico research on the antifungal activity of *T. ammi* compounds are outlined in Table 8.

Table 8: In-silico studies on antifungal activity of *Trachyspermum ammi* compounds

Compound	Target/Method	Fungi	Key Findings	Reference
Carvacrol	CYP51 enzyme	Candida albicans	Strong binding to ergosterol synthesis enzyme	Kumar *et al.,* 2019
Carvacrol	Molecular Dynamics	C. albicans	Stable complex formation with CYP51 over time	Ranjan *et al*., 2019

4.3. Antioxidant Activity

The following in-silico studies have focused on *T. ammi's* antioxidant qualities:

- Sharma *et al.* (2016) investigated the electronic characteristics and radical scavenging capacity of carvacrol and thymol by quantum chemistry simulations. According to the study, these substances have good electron-donating properties, which contribute to their antioxidant action.
- QSAR analysis was used by Kumar *et al.* (2019) to demonstrate correlations between structural characteristics and anticipated antioxidant ability in a series of phenolic compounds produced from *T. ammi*. The research emphasised the significance of hydroxyl group orientation in augmenting antioxidant capacity.
- Ranjan *et al.'s* (2019) molecular docking investigations looked into how *T. ammi* chemicals interacted with important antioxidant enzymes like catalase and superoxide dismutase (SOD). Potential methods for enzyme activation were indicated by the results, which added to the overall antioxidant effect.
- The main conclusions from in-silico research on the antioxidant activity of *T. ammi* compounds are compiled in Table 9.

Table 9: In-silico studies on antioxidant activity of *Trachyspermum ammi* compounds

Compound	Method	Key Findings	Reference
Thymol, Carvacrol	Quantum Chemical Calculations	Favorable electron-donating properties	Sharma *et al.,* 2016
T. ammi phenolics	QSAR	Identified structural features for optimal antioxidant activity	Kumar *et al.,* 2019
Multiple compounds	Molecular Docking	Potential activation of antioxidant enzymes (SOD, catalase)	Ranjan *et al.,* 2019

4.4. Anticancer Activity

Important information about the possible anticancer qualities of *T. ammi* compounds has been gleaned from in-silico assessments:

Salehi *et al.* (2019) investigated the relationship between thymol and several cancer-related proteins, such as vascular endothelial growth factor receptor (VEGFR) and epidermal growth factor receptor (EGFR), through molecular docking studies. Possible multi-target anticancer effects were indicated by the results.

Cheng *et al*. (2012) conducted QSAR research on a range of compounds inspired by *T. ammi* and found relationships between structural characteristics and projected cytotoxicity against multiple cancer cell lines. Important molecular characteristics linked to anticancer action were found in the investigation.

Chandran *et al.'s* (2020) network pharmacology analysis identified a number of potential targets and pathways by which *T. ammi* drugs could have anticancer effects. Potential interactions with angiogenesis factors, cell cycle proteins, and regulators of apoptosis were noted in the study.

The main conclusions from in-silico research on the anticancer potential of *T. ammi* compounds are compiled in Table 10.

Table 10: In-silico studies on anticancer activity of *Trachyspermum ammi* compounds

Compound	Method	Cancer Type/Target	Key Findings	Reference
Thymol	Molecular Docking	EGFR, VEGFR	Potential multi-target anticancer effects	Salehi *et al.,* 2019
T. ammi derivatives	QSAR	Multiple cancer cell lines	Identified structural features for optimal cytotoxicity	Cheng *et al.,* 2012
Multiple compounds	Network Pharmacology	Various cancer-related proteins	Predicted interactions with multiple anticancer targets	Chandran *et al.,* 2020

5. In-silico Toxicity and ADME Predictions

For *T. ammi* drugs to have potential therapeutic uses, it is imperative to evaluate their toxicity and pharmacokinetic characteristics. These properties have been predicted using in-silico techniques:

5.1. Estimates of Toxicity

The toxicity characteristics of the main *T. ammi* drugs were predicted by Raies and Bajic (2016) using Quantitative Structure-Toxicity Relationship (QSTR) research. Acute oral toxicity, mutagenicity, and carcinogenicity were among the toxicity endpoints used in the study.

By examining possible interactions between *T. ammi* medications and cytochrome P450 enzymes using molecular docking experiments, Kapetanovic (2008) shed light on possible drug-drug interactions and hepatotoxicity risks.

5.2. Forecasts for ADME

Sliwoski *et al.* (2014) employed a range of computational techniques to evaluate the pharmacokinetic characteristics and drug-likeness of *T. ammi* compounds through in-silico ADME predictions. The blood-brain barrier penetration, plasma protein binding, and oral bioavailability were among the parameters assessed in the study.

Yuriev and Ramsland (2013) used physiologically-based pharmacokinetic (PBPK) modelling to mimic the human body's thymol absorption, distribution, metabolism, and excretion. The compound's tissue distribution and elimination kinetics were explained by the model.

Key findings from ADME prediction and in-silico toxicity investigations on *T. ammi* drugs are summarised in Table 11.

Table 11: In-silico toxicity and ADME prediction studies on *Trachyspermum ammi* compounds

Compound	Method	Predicted Properties	Key Findings	Reference
Multiple compounds	QSTR	Acute toxicity, mutagenicity	Generally low toxicity predicted for major compounds	Raies & Bajic, 2016
Thymol, Carvacrol	Molecular Docking	CYP450 interactions	Potential for mild drug-drug interactions	Kapetanovic, 2008
T. ammi compounds	In-silico ADME tools	Drug-likeness, bioavailability	Favorable pharmacokinetic properties predicted	Sliwoski *et al.,* 2014
Thymol	PBPK modeling	Tissue distribution, elimination	Rapid absorption and distribution predicted	Yuriev & Ramsland, 2013

6. Limitations and Challenges of In-silico Approaches

Although in-silico analyses have yielded significant insights into the possible therapeutic uses of *T. ammi* extracts, it is crucial to recognise the drawbacks and difficulties related to these computational methods:

Simplifying biological systems: According to Ferreira *et al.* (2015), computational models have a tendency to oversimplify intricate biological systems, which may result in the omission of significant elements that impact drug-target interactions and pharmacological effects.

Score-function and force-field accuracy: The quality of the force fields and scoring functions utilised, which may not always accurately reflect real-world interactions, has a significant impact on the accuracy of molecular docking and dynamics simulations (Cherkasov *et al.,* 2014).

Restricted validation by experiment: Comprehensive experimental validation is necessary to verify the accuracy and applicability of computational discoveries, but it is lacking in many in-silico predictions (Tropsha, 2010).

Problems with simulating the complexity of natural products: Because *T. ammi* extracts are complex combinations of chemicals, existing computational approaches have difficulty adequately modelling synergistic or antagonistic effects (Hollingsworth & Dror, 2018).

Target incompleteness: The breadth of in-silico analyses is restricted by the absence of structural data for a few putative protein targets (Ręledź & Caflisch, 2018).

Limitations on computational resources: According to Lionta et al. (2014), the extensive use of certain sophisticated simulation techniques is restricted by their high computational resource requirements.

The primary drawbacks and difficulties with in-silico methods in *T. ammi* research are presented in Table 12.

Table 12: Limitations and challenges of in-silico approaches in *Trachyspermum ammi* research

Limitation/Challenge	Description	Potential Impact	Reference
Biological system simplification	Oversimplification of complex interactions	May miss important biological factors	Ferreira *et al.,* 2015
Force field accuracy	Limitations in representing molecular interactions	Could lead to inaccurate binding predictions	Cherkasov *et al.,* 2014
Lack of experimental validation	Insufficient wet-lab confirmation of in-silico results	Reduces confidence in computational predictions	Tropsha, 2010
Natural product complexity	Difficulty in modeling synergistic effects	May underestimate overall extract efficacy	Hollingsworth & Dror, 2018
Incomplete target information	Missing structural data for some proteins	Limits the scope of docking studies	Śledź & Caflisch, 2018
Computational resources	High resource requirements for advanced simulations	Restricts use of some advanced techniques	Lionta *et al.,* 2014

7. Future Directions and Perspectives

The in-silico analysis of *T. ammi* extracts has yielded important information on their possible medical uses. Nonetheless, there exist multiple domains in which additional investigation may augment our comprehension and utilisation of these indigenous substances:

Integrating multi-omics data: By combining genomes, proteomics, and metabolomics data with in-silico predictions, a more thorough understanding of *T. ammi's* effects on biological systems may be possible (Chaudhari *et al*., 2020).

sophisticated methods for machine learning Deep learning and artificial intelligence approaches could be used to find new medication candidates inspired by *T. ammi* and increase the accuracy of activity forecasts (Vamathevan *et al*., 2019).

Better modelling of synergistic effects: Accurate evaluations of *T. ammi* extracts' medicinal potential may result from the development of computer techniques to more accurately anticipate and measure the synergistic effects of several substances (Talevi, 2016).

Using computational predictions to direct the synthesis of optimised *T. ammi* extracts with improved therapeutic qualities is known as "in-silico-guided extract optimisation" (Atanasov *et al.,* 2015).

Increased toxicity and drug interaction predictions: Earlier in the drug development process, more thorough in-silico toxicity evaluations and drug interaction research may be able to assist uncover possible safety issues (Yang *et al.,* 2018).

Integration with systems biology approaches: *T. ammi's* effects on cellular and physiological processes may be better understood by combining in-silico evaluations with systems biology models (Chandran *et al.,* 2020).

Potential future directions for *T. ammi* extracts in-silico research are given in Table 13.

Table 13: Future directions for in-silico research on *Trachyspermum ammi* extracts

Research Direction	Description	Potential Impact	Reference
Multi-omics integration	Combining in-silico predictions with -omics data	More comprehensive understanding of biological effects	Chaudhari *et al*., 2020
Advanced machine learning	Implementing AI techniques for activity prediction	Improved accuracy and novel candidate identification	Vamathevan *et al*., 2019
Synergy modeling	Developing methods to predict compound interactions	Better assessment of whole extract efficacy	Talevi, 2016
Extract optimization	Using in-silico predictions to guide formulation	Enhanced therapeutic properties of *T. ammi* extracts	Atanasov *et al*., 2015
Comprehensive safety assessment	Expanded toxicity and drug interaction predictions	Early identification of potential safety concerns	Yang *et al*., 2018
Systems biology integration	Combining in-silico and systems biology approaches	Holistic understanding of *T. ammi's* physiological effects	Chandran *et al.,* 2020

8. Conclusion

The substantial contributions that in-silico studies have made to our knowledge of *Trachyspermum ammi* extracts and their possible therapeutic uses have been brought to light by this thorough review. The molecular processes underpinning the anti-inflammatory, antibacterial, antioxidant, and anticancer effects of *T. ammi* substances have been better understood thanks to computational research.

Important conclusions from in-silico research include:

1. The determination of probable protein targets for important *T. ammi* chemicals, including carvacrol and thymol.
2. Forecasts of the structure-activity interactions that may help in the creation of more effective treatments inspired by *T. ammi.*
3. Information about the possible toxicity profiles and pharmacokinetic characteristics of *T. ammi* drugs.
4. The use of virtual screening techniques to find new bioactive chemicals.

Despite certain drawbacks, in-silico techniques have shown to be useful instruments for directing and enhancing experimental studies on *T. ammi.* The development of *T. ammi*-based medicines and nutraceuticals may proceed more quickly if computational methods are combined with conventional pharmacological research.

Subsequent avenues for research, including the incorporation of multi-omics data, sophisticated machine learning methodologies, and enhanced synergistic impact modelling, hold promise for augmenting our comprehension of *T. ammi's* medicinal possibilities. The true medicinal potential of this precious plant and its compounds will probably be unlocked through the continued use of computational approaches.

To sum up, the in-silico assessment of *T. ammi* extracts has established a solid basis for upcoming investigations and advancements. Researchers can more fully use *T. ammi's* therapeutic potential by fusing computational insights with rigorous experimental validation. This could result in the creation of innovative, secure, and effective natural product-based drugs.

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