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Therapeutic potential of fruit crop phytochemicals: An *in silico* drug discovery perspective

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Abstract

Fruit crops serve as a vital natural source of biologically active phytochemicals that play an important role in enhancing human health. These naturally occurring substances are widely studied because of their potential in preventing and treating a variety of diseases. With advancement in computational approaches in drug discovery, scientists can now more effectively identify and analyze bioactive molecules derived from fruits. Phytochemicals such as polyphenols, flavonoids, terpenoids, carotenoids, alkaloids and sulfur-based compounds exhibit a broad spectrum of pharmacological properties. Many of these compounds possess antioxidant, anti-inflammatory, antiviral, anticancer and neuroprotective activities. They affect numerous molecular targets and cellular signalling pathways involved in the initiation and progression of diseases. In recent years, advanced *in silico* drug discovery techniques, including molecular docking, molecular dynamics simulations, pharmacokinetic analysis and network pharmacology, have enabled rapid screening and evaluation of natural compounds to evaluate their potential therapeutic benefits. These computational methodsenable researchers to predict ligand-protein interactions, drug-likeness and toxicity profiles before conducting experimental studies, thereby reducing the time and cost associated with traditional drug discovery processes. Several fruit crops, such as *Musa acuminata* (banana), *Vitis vinifera* (grape), *Punica granatum* (pomegranate), *Mangifera indica* (mango) and *Citrus sinensis* (orange) are rich in bioactive compounds including dopamine, resveratrol, ellagitannins, mangiferin and hesperidin. These molecules have demonstrated promising biological activities against key disease targets such as viral enzymes, inflammatory mediators, metabolic regulators, and cancer-related signalling pathways. Although, phytochemical research has been accelerated by various approaches, difficulties persist in ensuring accuracy of predictions and validating experimental findings. Even so, artificial intelligence, metabolomics and advanced molecular modelling are anticipated to contribute to the development of more efficient natural product-based drug discovery from fruit crops in the future.

1. Introduction

Fruit is a crucial component of the human diet, as it provides essential nutrients, antioxidants and dozens of bioactive elements. The crops are highly nutritious. In addition to their nutritional value, fruits contain a range of secondary metabolites that display significant pharmacological properties. These compounds, which are naturally occurring, have been the subject of much research in health and biomedical fields due to their numerous biological functions. These phytochemicals have been identified as essential for the protection of plants from pathogens, environmental stress and herbivory, while also offering health benefits to humans when consumed (Singh *et al.,* 2016). Phytochemicals in fruits are believed to have beneficial effects on chronic conditions, including cancer, cardiovascular disorders, diabetes, neurodegenerative diseases and viral infections (Narayanakutty *et al.,* 2024). Fruits have been found to contain a wide range of bioactive compounds, including flavonoids, phenolic acids and tannins; carotenoids (especially citrus fruits), terpenoids or alkaloids; as well as various phytochemical studies. Many people now know these compounds for their biological value and potential health benefits. Several biological activities are demonstrated by these compounds, including antioxidant, anti-inflammatory, and antimicrobial, as well as anticancer effects (Kumar *et al.,*2013). Similarly, hesperidin found in citrus fruits has shown antiviral and anti-inflammatory potential in several studies. Traditional drug discovery methods based on natural products are often time-consuming and expensive because they require extensive laboratory screening and experimental validation (Wu *et al*., 2020). However, the emergence of *in silico* drug discovery techniques has transformed the process of identifying therapeutic molecules. Computational approaches such as molecular docking, molecular dynamics simulations, pharmacokinetic prediction and network pharmacology allow researchers to efficiently analyze the disease-associated biological targets, facilitating the identification of potential therapeutic

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compounds (Singh*et al*., 2021). These computational approaches help minimize the time and financial resources needed in the drug discovery process by enabling the rapid screening, evaluation of large compound libraries.

The integration of computational biology with phytochemical research has enabled the rise of Computer-Aided Drug Design (CADD) methods, which are widely used in contemporary pharmaceutical research for discovering and developing potential therapeutic agents. These methods consist of structure-based drug design and ligand-based drug design, which assist in forecasting the binding affinity of natural compounds to target proteins implicated in disease pathways (Chen *et al*., 2020). In recent years, multiple studies have employed these computational tools to recognize fruit-derived phytochemicals as possible blockers of viral proteins, cancer-causing signalling pathways and metabolic enzymes. Network pharmacology methods have shown that natural substances frequently display interactions with multiple targets, which enhances their effectiveness in addressing intricate diseases that engage several biological pathways (Zhang *et al*., 2019). Consequently, fruit phytochemicals serve as a significant resource for creating safer and more effective therapeutic compounds. The review outlines various biochemical characteristics of fruit metabolites, along with their pharmacological effects, computational techniques for drug discovery, case studies demonstrating their potential in combating significant illnesses.

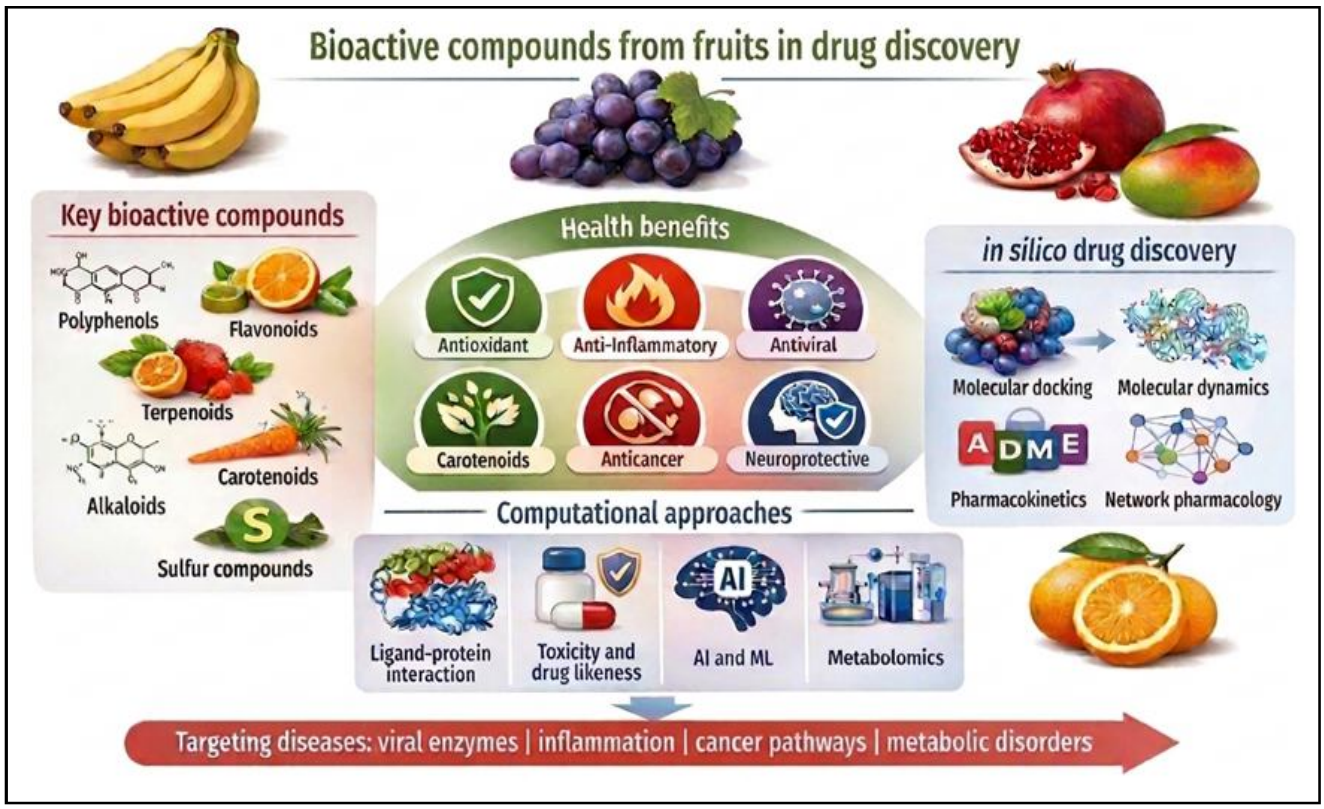

Figure 1: Graphical abstract of fruit-derived bioactive compounds in drug discovery, from phytochemical identification to computational modelling for disease targeting.

2. Phytochemical diversity in fruit crops: Biochemical and functional perspectives

Fruit crops contain a complex group of secondary metabolites that are essential for both plant and human health. The flavor, color, aroma and medicinal properties of fruits are enriched by the production of these metabolites through specialized biosynthesis. The extensive pharmacological activities of phytochemicals obtained from fruit crops and their potential for use in natural product-based drug discovery have garnered considerable attention. Phytochemical diversity in fruits is caused by differences in plant species, genetic factors and environmental conditions as well as the way they are handled after being harvested. Hundreds of bioactive substances in fruit tissues have been identified through the use of modern analytical techniques, such as liquid chromatography-mass spectrometry (LC-MS) and nuclear magnetic resonance spectra (Sarkar *et al*., 2025). These compounds are broadly divided into groups of phenolics, terpenoids and alkaloids as well as other nitrogen-containing metabolites. Phytochemicals from fruits are typically classified by their chemical structure and biosynthesis processes. Among these, phenolic compounds are one of the most common groups and have subclasses such as flavonoids, tannins and primarily acetic acids. These compounds are widely acknowledged for their antioxidant properties, particularly in the reduction of reactive oxygen species and protection of cellular structures against oxidative stress (Kaur *et al*., 2001). The majority of flavonoids, such as quercetin, catechin and anthocyanins are found in fruits like grapes or berries, but they also have anti-inflammatory and anticancer effects. Tannic and phenolic acids have been found to have significant antimicrobial and cardiovascular benefits (Nardini, 2022).Terpenoids and carotenoids,

are the major vital phytochemicals found in fruits. Many fragrant compounds found in fruits are created from isoprene units as their terpenoids. Beta-carotene, lutein and lycopene are carotenoids that are crucial for human health, serving as vitamin A precursors and providing antioxidant protection against oxidative stress (Maji *et al*., 2025).

2.1 Biosynthetic pathways of therapeutically active compounds

The production of phytochemicals in fruits is supported by several metabolic pathways, such as the shikimate pathway, phenylpropanoid pathway and isoprenoid pathway. The generation of phenolic compounds, terpenoids, and various secondary metabolites relies on these biochemical pathways. The generation of phenolic compounds, such as flavonoids and tannins is mainly influenced by the shikimate and phenylpropanoid pathways. These routes allow for the conversion of simple carbohydrates into aromatic amino acids, which subsequently transform them into intricate phenolic compounds with strong antimicrobial and antioxidant characteristics (Ninkuu *et al*., 2025).The mevalonate and methylerythritol pathways are involved in the synthesis of terpenoids and carotenoids. These metabolic routes produce isoprenoid precursors, which are later transformed into a variety of bioactive substances that contribute to the plant's defense and stress response (Wang *et al*., 2025). Genetic influences, environmental pressures and the developmental phase of the fruit would impact these biosynthetic pathways. Advancements in plant genomics have enabled the identification of essential enzymes and regulatory genes that govern phytochemical production, potentially enhancing the medicinal benefits of fruit crops.

2.2 Major fruit crops as phytochemical reservoirs

Phytochemicals present in fruit crops are plentiful and varied, carrying therapeutic benefits. The secondary metabolic pathways in plants generate these compounds, which mainly serve as protective agents to defend plants against environmental stresses, microbial pathogens and herbivorous organisms. Concerning human health, phytochemicals exhibit various pharmacological properties, such as antioxidant (some anti-inflammatory), anticancer, antiviral and neuroprotective effects. Multiple widely cultivated fruit crops have been recognized as beneficial sources of biologically active substances, crucial for drug discovery based on natural products and the development of nutraceuticals (Kumar *et al*., 2023). The phytochemical variety of banana (*M. acuminata*) ranks as one of the most significant among these fruit crops. Bananas contain bioactive constituents such as phenolic compounds, dopamine derivatives, catecholamines, flavonoids and carotenes. Dopamine, present in both the flesh and peel of bananas, acts as a powerful antioxidant that can neutralize reactive oxygen species and protect cellular components from oxidative damage. Banana catecholamines have been shown to exhibit anti-inflammatory and cardioprotective properties by modulating oxidative stress-related pathways (Ali *et al*., 2023). Moreover, banana peels are rich in phenolic acids and flavonoids, which have been evaluated in clinical trials for their potential to prevent cancer and fight microorganisms. In addition, Grape (*V. vinifera*) is a fruit that possesses considerable therapeutic worth as a pharmacologically relevant substance. Resveratrol, quercetin, catechins and anthocyanins are among the polyphenolic compounds found in grapes. Resveratrol has received significant interest because of its potential to provide cardioprotective properties, anticancer characteristics and antiageing effects. NF-B pathway, PI3K/Akt pathway and sirtuin signalling are among the many cellular signalling pathways modulated by this compound (Zhou *et al.*, 2021). These pathways are involved in inflammation and cell survival. Flavonoids from grapes possess potent antioxidant properties, which have been extensively researched to prevent neurodegenerative diseases such as Alzheimer's and Parkinson's. *P. granatum*, also known as pomegranate, is rich in ellagitannins and punicalagins, which are bioactive phytochemicals. These compounds are primarily responsible for the anti-inflammatory and anticancer effects of pomegranate extracts, as they possess significant antioxidant properties. Pelaginannins derived ELAGIC acid is known to inhibit tumor growth by stimulating cell division, specifically apoptosis and angiogenesis in certain cancer types (Noreen *et al*., 2025).The polyphenolic compound mangiferin found in mango (*M. indica*) is one of the phytochemicals that make it highly valued. Mangiferin exhibits antioxidant effects, anti-inflammatory properties, antiviral traits and benefits related to diabetes. Several studies indicate that mangiferin can regulate glucose metabolism by modulating insulin signalling pathways and inhibiting carbohydrate-hydrolysis enzymes like amylase and elongated glucose (Jahnavi *et al*., 2020). Citrus fruits, like orange (*C. sinensis*), lemon, and grapefruit, play important roles in generating pharmacologically active phytochemicals. Hesperidin, naringin and rutin are some of the flavonoids present in citrus fruits. Other significant carotenoids consist of carotenoid substances. Hesperidin has been shown to possess anti-inflammatory and antiviral effects by modulating cytokine production and inhibiting inflammatory signaling pathways (Denaro *et al*., 2021). Berries are rich in anthocyanins and flavonoids, which possess antioxidant and anti-inflammatory properties. Quercetin and chlorogenic acid, present in apples, are associated with cardiovascular health and metabolic advantages (Mareri *et al*., 2022). The variety of phytochemicals found in fruit crops underscores their significance as natural sources of medicinal compounds. Improvements in metabolomics and phytochemical analysis methods have allowed scientists to discover and describe many bioactive compounds from fruits (Manickam *et al*., 2023). Moreover, computational drug discovery techniques have incorporated phytochemical databases to pinpoint fruit-sourced molecules as possible drug candidates for addressing complex illnesses. To summarize, fruit crops serve as a valuable resource for investigating natural products due to their varied biological functions and rich phytochemical content (Zhang *et al*., 2019).

2.3 Genotype, environment, and postharvest handling have an impact on phytochemical profiles

Genetic variation in fruit cultivars affects the concentration and diversity of phytochemicals. The production and build-up of secondary metabolites, including flavonoids, phenolic acids, carotenoids and terpenoids, can vary greatly between different fruit species because of their unique genotype. Genetic variations stem from differing expression patterns of metabolic enzymes and regulatory genes that control biosynthetic pathways for phytochemicals (Mieszczakowska-Frac *et al*., 2025). The antioxidant properties and potential health benefits of grape varieties are heavily influenced by their high levels of resveratrol and anthocyanin, which differ from one another. The quantity of mangiferin and carotenoids in mango pulp and peel varies greatly, which is also the case for other types. Some studies have shown that some banana varieties exhibit higher levels of dopamine and phenolic compounds than others,

suggesting that genetic diversity is an important factor in determining the medicinal value of fruit crops (Atanasov *et al*., 2021; Zhou *et al*., 2021).

Environmental factors including temperature, light intensity, rainfall patterns and soil composition play a significant role in influencing the production of secondary metabolites in fruit crops. In response to environmental stressors like drought, UV radiation and pathogen presence, plants frequently increase the production of protective phytochemicals as a component of their adaptive defense strategies. Responses triggered by stress activate metabolic pathways that lead to the synthesis of antioxidants and various protective compounds (Ogwu *et al*., 2025). Flavonoids and anthocyanins are recognized to form in fruits when they are exposed to sunlight. Grapes exhibit increased antioxidant properties when cultivated in more intense sunlight, leading to elevated amounts of anthocyanins and polyphenols. Phenolic compounds are incorporated into fruit tissues, a response by the plant as an adaptive defense mechanism against environmental stress like water shortage. The presence of soil nutrients, minerals and the levels of nitrogen can influence phytochemical accumulation, synthesis of alkaloids and phenolic compounds (Chen *et al*., 2020).

The stability and availability of phytochemicals in fruits are significantly influenced bypostharvest handling and storage conditions. The levels of bioactive compounds can significantly be influenced by factors like harvesting time, storage temperature, transportation techniques (like vaporization or nitrogen) and processing. The healing properties of fruits can be reduced because sensitive compounds such as vitamin C, anthocyanins and carotenoids degrade when stored in unsuitable condition (Arendse *et al*., 2014). Fruits are often kept in cold storage to extend their freshness, yet prolonged refrigeration may lead to metabolic changes that affect their phytochemical makeup. The oxidative breakdown of bioactive compounds during storage is reduced by the levels of oxygen and carbon dioxide in controlled atmosphere storage systems. The stability of phytochemicals can be affected by drying, juicing or thermal processing techniques (Camara *et al.*, 2020).

3. Therapeutic relevance of fruit phytochemicals

Phytochemicals that come from fruits have generated significant scientific interest due to their broad pharmacological activities and potential role in preventing and managing various human diseases. Bioactive compounds interact with various molecular targets and cellular pathways that control inflammation, immune responses, cell division and stress (Zaky *et al*., 2024). In addition, several fruit phytochemicals including flavonoids, phenolic compounds and terpenoids have important biological functions such as antioxidant, anti-inflammatory, viral, cancer suppressant and neuroprotective effects, which make them more valuable for therapeutic purposes (Kotha *et al*., 2022; Alam *et al*., 2022). Additionally, progress in molecular biology and computational pharmacology has resulted in an improved comprehension of how these substances affect the moles associated with disease mechanisms. Thus, the utilization of fruit-derived phytochemicals is gaining traction as possible lead compounds in drug discovery *via* natural products. These substances are recognized for their ability to target multiple sites, allowing them to control several biochemical pathways at once. Unlike conventional synthetic medications that usually focus on a single molecular target, natural phytochemicals can engage with intricate biological networks associated with multifactorial diseases (Rudzinska *et al*., 2023). Additionally, their ability to modulate multiple signalling pathways enhances their therapeutic efficacy while minimizing the risk of resistance formation. In general, the broad biological activities and multi-target interactions associated with fruit phytochemicals indicate their great potential as potential natural therapeutic agents for future pharmaceutical development (Lal *et al*., 2022).

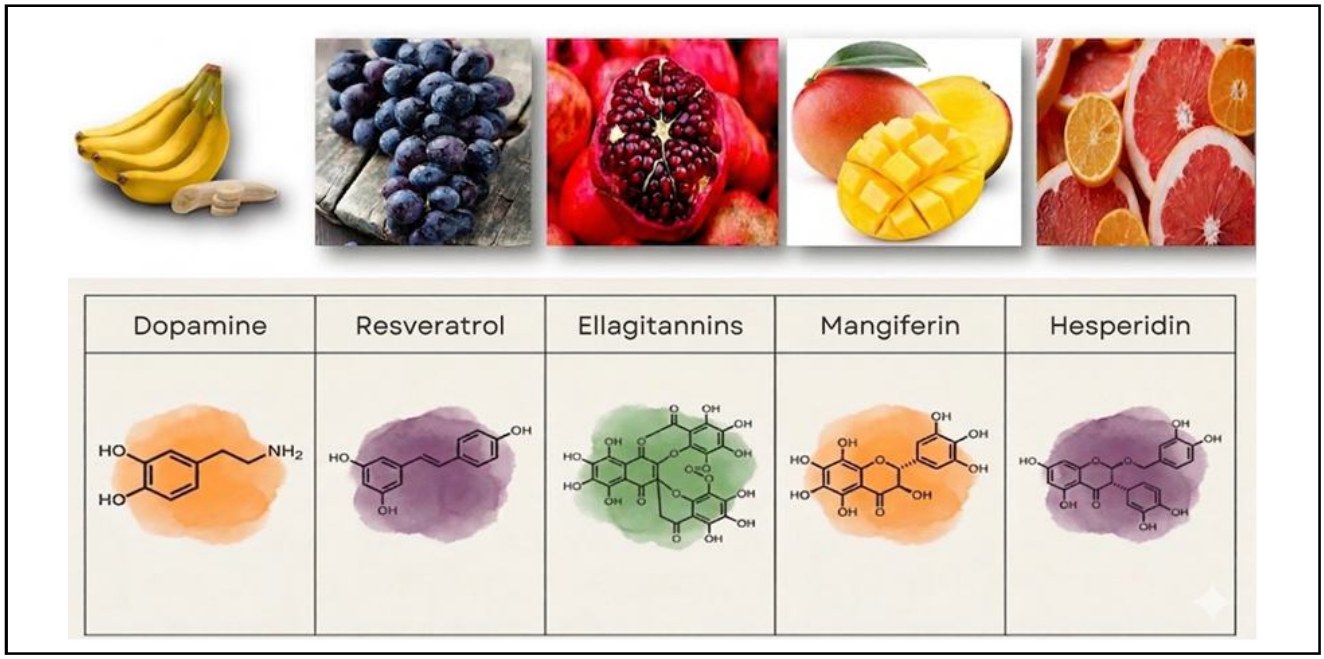

Figure 2: Chemical diversity of key dietary secondary metabolites and their representative fruit sources, including dopamine (banana), resveratrol (grape) and mangiferin (mango).

3.1 Antioxidant and anti-inflammatory mechanisms

Fruit phytochemicals are essential in protecting the body from oxidative stress and inflammation, which contribute to many chronic diseases. In humans, reactive oxygen species (ROS) that exceed the antioxidant defense system's capacity causes oxidative stress and damages DNA, proteins or lipids in the cell (Muscolo *et al*., 2024). Among the natural antioxidants in fruit are flavonoids, phenolic acids and carotenoids; these substances help counteract free radical damage by acting as natural neutralizing agents for freeradical molecules. In addition, compounds such as resveratrol, quercetin and catechin have been found to increase the activity of antioxidant enzymes like superoxide dismutase, catalase or glutathione peroxidases, which are responsible for maintaining cellular rearithm (Rudrapal *et al*., 2024; Jain *et al*., 2025). Additionally, numerous phytochemicals derived from fruits exhibit noteworthy anti-inflammatory effects by modulating molecular pathways involved in immune regulation. These compounds have been shown to inhibit the nuclear factor kappa B (NF-B) signalling pathway, which is responsible for controlling pro-inflammatory cytokines such as TNFα, IL-1 and µl-6 (Wu *et al*., 2022; Chauhan *et al*., 2022). Moreover, certain polyphenols found in fruits like grapes and berries have been shown to inhibit inflammatory signalling pathways and reduce tissue damage, while others such as hesperidin in citrus fruits can regulate immune responses and decrease the production of inflammation mediators (Poojari *et al*., 2025). Hence, the antioxidant and anti-inflammatory effects of fruit phytochemicals are crucial in their protective properties against various diseases, including cardiovascular disorders, cancer and metabolic syndrome.

3.2 Anticancer potential

Fruit-derived phytochemicals have been identified as natural anticancer agents due to their ability to regulate various cellular pathways that play a role in tumour growth. The compounds have multiple functions, including the inhibition of cell division, suppression of angiogenesis and inducing apoptosis (Atanasov*et al*., 2021; Monica *et al*., 2025). In addition, apoptosis is an essential process that eliminates abnormal or damaged cells and various phytochemicals such as resveratrol, aloecnica, mangiferin, *etc*., have been found to activate caspase enzymes that trigger programmed cell death in cancer cells (Morozkina *et al*., 2021). However, these compounds have the ability to regulate cyclin-dependent kinases and induce cell cycle arrest, which can prevent uncontrolled cancer cell growth (Farhan *et al*., 2023). Also, fruit phytochemicals have the potential to hinder angiogenesis, the process by which tumours generate new blood vessels to ensure their growth and survival. Inhibition of vascular endothelial growth factor (VEGF) signalling by polyphenolic compounds, including quercetin and resveratrol, has been observed in certain studies (Ren *et al*., 2021; Islam *et al*., 2025).

3.3 Antiviral and antimicrobial activities

Phytochemicals that come from fruits exhibit notable antiviral and antimicrobial properties, which could lead to the development of new therapeutic agents for treating infectious diseases. Key viral enzymes, such as proteases, polymerases and helicases are targets of numerous natural compounds that inhibit replication (Han *et al*., 2023). Studies in recent years have highlighted the antiviral properties of flavonoids and Polyphenols, which have been found to be effective against several viruses, including human immunodeficiency virus (HIV) and Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). Molecular docking analyses have revealed that quercetin, hesperidin and catechin can inhibit the entry and replication processes by binding to viral proteases and spike proteins.In addition to their antiviral properties, phytochemicals from fruits demonstrate considerable antibacterial effects by compromising bacterial cell membranes, blocking crucial enzymatic functions, and disrupting cellular interactions via metabolic pathways in bacteria like quorum sensing (Mani *et al*., 2020; Jo *et al*., 2020). Reports indicate that pomegranate and grape extracts have phenolic compounds capable of suppressing the growth of harmful bacteria, such as *Staphylococcus* and *Escherichia* (Ghildiyal *et al*., 2020). Moreover, bacterial efflux pumps that contribute to antibiotic resistance in numerous bacterial strains can be targeted by another significant antimicrobial mechanism. By obstructing these transport mechanisms, fruit phytochemicals can improve the effectiveness of standard antibiotics and assist in curbing the rise of drug-resistant bacteria (Silva *et al*., 2016; Salim *et al*., 2023).

3.4 Metabolic and neuroprotective effects

Phytochemicals derived from fruits are crucial in regulating metabolic processes and offer neuroprotective benefits against neurodegenerative diseases. Various bioactive compounds extracted from fruits have demonstrated antidiabetic properties by inhibiting critical enzymes involved in carbohydrate breakdown and glucose metabolism. For example, flavonoids and phenolic acids can inhibit enzymes such as α-amylase and α-glucosidase, which are responsible for the breakdown of carbohydrates into glucose (Febriyanti *et al*., 2025).In addition to enzyme inhibition, fruit-derived phytochemicals can enhance insulin sensitivity and regulate glucose uptake in peripheral tissues. Compounds such as mangiferin from mango and resveratrol from grapes have been reported to activate AMP-activated protein kinase, an important regulator of cellular energy metabolism. Similarly, guava (*P. guajava*) is abundant in a wide range of phytochemicals, particularly flavonoids like quercetin, kaempferol, myricetin and rutin, as well as phenolic acids including gallic, caffeic and chlorogenic acids. It also contains triterpenoids such as oleanolic, ursolic and betulinic acids, along with essential oil components like β-caryophyllene and α-terpineol. These compounds collectively contribute to its diverse biological properties, including antioxidant, antidiabetic and neuroprotective effects. Mechanistically, they regulate metabolic processes by modulating key carbohydrate-metabolizing enzymes, improving insulin sensitivity, which enhances glucose uptake and maintains energy homeostasis. Additionally, its neuroprotective potential is attributed to pentacyclic triterpenoids that can cross the blood-brain barrier, inhibit acetylcholinesterase, and reduce amyloid plaque formation, ultimately supporting cognitive function (Kumar *et al*., 2021; Hanh *et al*., 2025). Fruit phytochemicals have been extensively reported to possess neuroprotective properties. It is widely recognized that neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease are in part caused by oxidative stress and inflammatory responses (Yang *et al*., 2021; Martiz *et al*., 2023; Li *et al*., 2025). The antioxidant elements in fruits can safeguard neuronal cells by minimizing oxidative harm and enhancing internal cellular defense mechanisms. Additionally, certain phytochemicals obtained from fruits have demonstrated the ability to hinder the enzyme acetylcholinesterase, which degrades the neurotransmitter ACETYLCHOLINE. Blocking this enzyme improves

cognitive abilities and memory in people with neurodegene-rative diseases. Research findings have demonstrated that quercetin, anthocyanins and various other compounds exhibit significant neuroprotective effects (Godos *et al*., 2021; Bagrowska *et al*., 2024; Bej *et al*., 2024).

4. *In silico* drug discovery approaches in phytochemical research

Extensive experimental screening, compound isolation and biological validation have been the customary methods for discovering therapeutic agents from natural products, but these processes are often time-consuming and resource intensive. However, advances in computational biology have made this process significantly different. By combining computational tools with phytochemical research, *in silico* drug discovery approaches (Rodrigues *et al*., 2020), the identification of promising bioactive molecules can be expedited. In addition, there is a vast selection of natural compounds from fruit crop phytochemicals that can be evaluated efficiently using these computational methods. Predicting interactions between phytochemicals and disease-related targets using molecular docking, molesimization, pharmacokinetic modelling and network pharmacology is possible for researchers before laboratory validation (Maia *et al*., 2020; Khemnar *et al*., 2021). Besides, these methods enable speedy screening of substantial library of compounds and the identification of molecules with strong binding affinity (Burley *et al*., 2022). Traditional drug discovery processes are made more efficient and cost-effective by computational screening. The utilization of computational methods in addition to phytochemical studies presents a practical method for investigating plant substances and expediting the progress of modern drugs (Yu *et al*., 2017).

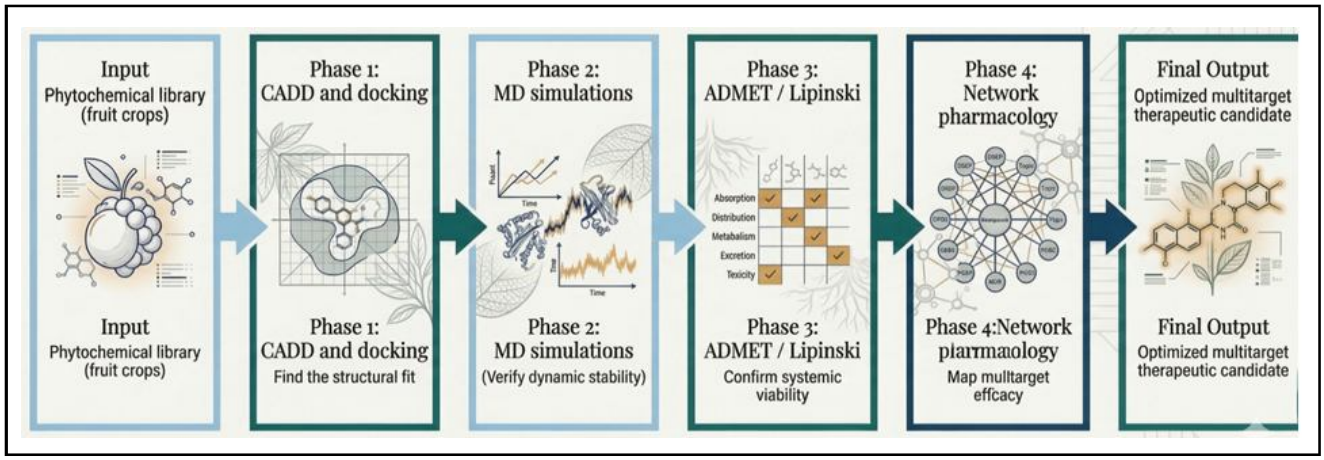

Figure 3: A systematic pipeline for *in silico* drug discovery from fruit-derived phytochemicals, integrating molecular docking, dynamic simulations and ADMET profiling for multi-target therapeutic optimization.

4.1 Computer aided drug design overview

Computer-aided drug design [CADD] is a computational approach that aids researchers in identifying and optimizing drug candidates. By utilizing concepts from structural biology, bioinformatics, and computational chemistry, it endeavour to understand the interactions between chemical molecules and biological targets, biological interactions. With this integrated approach, scientists can create and analyze potentially therapeutic molecules with increased efficiency and precision. Two main approaches to CADD are SBDD (Structure based drug design) and LBDS (ligand-based drug design) (Sliwoski *et al*., 2013; Vamathevan *et al*., 2019). Structure-based drugs are designed by utilizing the three-dimensional structure of target proteins to identify binding sites for potential drug molecules. The Protein Data Bank and other databases are used to store structural information, which is typically obtained through experimental methods like X-ray crystallography or nuclear magnetic resonance spectroscopy (Sadybekov *et al*., 2023). Ligand-based drug development is cantered on the examination of bioactive molecules that interact with specific biological targets. The creation of novel compounds with enhanced pharmacological effects relies on these traits. Both SBDD and LBDD approaches have effectively screened fruit-based phytochemicals for disease-associated targets, such as viral enzyme activity, inflammatory mediators and metabolic regulators. These strategies allow researchers to pinpoint drug candidates that demonstrate excellent specificity and minimal toxicity (Burley *et al*., 2022)

3.2 Molecular docking studies

Molecular docking is a computational method commonly employed in drug discovery that predict show small molecules (like phytochemicals) interact with particular target proteins on a molecular scale. This technique can be employed to ascertain the binding orientation, interaction energy and stability of ligand-protein complexes (Pinzi *et al*., 2019). The docking procedure usually begins with obtaining, from structural databases, the 3-dimensional structure of the target protein and then preparation steps such as removing water molecules and optimizing amino acid residues. Furthermore, the ligand configuration is refined for precise interaction evaluation. Docking algorithms analyze various binding conformations and employ scoring functions to assess binding affinity (Ferreira *et al*., 2015). Lower binding energy values in compounds suggest enhanced interactions with the target protein. The use of molecular docking in fruit-derived phytochemicals, such as quercetin, hesperidin and other antioxidant against viral, interferon-targeting targets and cancer-related drugs has also been widely used. In essence, this technique provides valuable insights into molecular interactions and assists in identifying promising therapeutic candidates from natural compounds (Torres *et al*., 2019; Singh *et al*., 2025; Mirgaux *et al*., 2026)

4.3 Molecular dynamics simulations

The study of molecular docking provides crucial insights into ligand and protein interactions, but it is only a static representation of binding. Proteins and ligands are structural components of biological systems that undergo constant conformational changes. Molecular dynamics (MD) simulations are employed to assess the stability and behaviour of ligand-protein complexes in physiological contexts (Salo *et al*., 2021; Garduno *et al*., 2024). Furthermore, MD simulations employ the principles of classical mechanics to analyze the evolution of atoms in a molecular system over time, enabling researchers to verify interaction stability in an artificial biological environment. Moreover, various parameters are frequently examined during simulations, such as root mean square deviation (RMSD), which measures structural stability and root mean square fluctuation (RMSF), that indicates the adaptability of amino acid residues (Filipe *et al*., 2022; Vieira *et al*., 2023). Moreover, the ability to dissolve hydrogen bonds and access to solvents are evaluated to determine the strength of an adhesive bonding mechanism. The use of MD simulations is common to verify molecular docking results and confirm the stability of phytochemicals like resveratrol and quercetin when bound to proteins associated with disease (Paul *et al*., 2021).

4.4 ADMET and pharmacokinetic profiling

It is important to consider both the binding affinity and pharmacokinetic properties of compounds to determine if they can be classified as effective drugs. Chemical compounds' absorption, distribution, metabolism, excretion, and toxicity properties are the focus of ADMET analysis (Daina *et al*., 2017). AdmoMet tools rely on computational methods to predict the chemical structure of a compound in the human body. By using these predictions, researchers can identify potential issues related to bioavailability, toxicity or metabolic instability before performing laboratory tests (Jia *et al*., 2020). Lipinski's Rule of Five, a well-known guideline for drug discovery, is commonly used to determine the drug-likeness of chemical compounds. The regulation states that a compound's molecular weight, lipophilicity, hydrogen bond donors and hydrogen link acceptors are essential for its optimal oral bioavailability. The pharmacokinetic traits of fruit-based phytochemicals are often well-suited to their natural composition and structural variation. Using computational ADMET analysis, scientists can identify compounds with drug-like properties and select promising candidates for further experimental investigation (Fan *et al*., 2025; Ancuceanu *et al*., 2025).

5. Computational assessment of fruit phytochemicals in response to emerging ailments

The application of computational approaches in natural product research has significantly enhanced the exploration of fruit-derived phytochemicals as potential therapeutic agents. Computational *in silico* techniques, including molecular docking, molecular dynamics simulations, and network pharmacology, have enabled researchers to investigate the interactions between fruit-derived phytochemicals and molecular targets associated with various diseases. These approaches provide valuable insights into the mechanisms through which natural compounds exert therapeutic effects and help identify promising candidates for further experimental validation (Atanasov *et al*., 2021; Fu *et al*., 2025). Fruit phytochemicals have demonstrated potential activity against several emerging diseases including viral infections, cancer, metabolic disorders and inflammatory diseases. By analyzing the binding interactions between phytochemicals and disease-related proteins, researchers can identify compounds that may act as inhibitors of critical biological pathways involved in disease progression (Wang *et al*., 2025)

Table 1: Bioactive phytochemicals from fruit crops and their therapeutic potential: Disease model, computational approaches, and mechanistic insights

S. No.	Fruit crop	Phytochemical	Disease model	Computational approaches and mechanistic insights	References
1.	Grape (*V. vinifera*)	Resveratrol	Viral (COVID-19)	Molecular Docking, MD simulation, Competitive inhibition of viral protease	Pandey *et al*., 2021
2.	Pomegranate (*P. granatum*)	Ellagic acid	Viral/cancer	Docking, MD simulation, Network pharmacology, Pathway enrichment. Inhibits viral entry; induces apoptosis *via*Akt pathway suppression	Noreen *et al*., 2025
3.	Citrus (*C. sinensis*)	Hesperidin	Viral/inflammatory	Docking, ADMET, Molecular dynamics, QSAR. Blocks spike_ACE2 interaction; suppresses inflammatory signaling	Khan *et al*., 2020
4.	Mango (*M. indica*)	Mangiferin	Metabolic (Diabetes)	Docking, MD simulation, ADMET, Pharmacophore modelling. Enhances insulin sensitivity; inhibits carbohydrate hydrolysis enzymes	Sekar *et al*., 2019
5.	Banana (*Musa* spp.)	Dopamine derivatives	Cancer /inflammation	Docking, Network pharmacology, Molecular dynamics. Antiangiogenic activity; Modulation of inflammatory cytokine signaling	Ferrari *et al.,* 2023

5.1 Viral diseases

Viral illnesses continue to be a major global health concern, especially with the rise of new viral pathogens like SARS-CoV-2. The progress of antiviral medications is frequently obstructed by viral mutations and resistance to drugs. Natural substances obtained from fruits have demonstrated encouraging antiviral effects by influencing viral enzymes and structural proteins essential for viral replication and entry into host cells (Adeosun *et al*., 2024). Numerous computational

analyses have examined fruit phytochemicals as possible blockers of viral proteins including the main protease (Mpro), RNA-dependent RNA polymerase (RdRp) and spike proteins. Molecular docking investigations have shown that flavonoids like quercetin and hesperidin can effectively attach to the active sites of viral proteases, thus hindering viral replication (Aguiar *et al*., 2025; Ren *et al*., 2025). The antiviral potential of polyphenolic compounds found in grapes and berries has also been explored. These findings suggest that fruit-derived phytochemicals may serve as potential antiviral agents for the treatment of emerging viral diseases (Santhi *et al*., 2021; Mehta *et al*., 2024)

5.2 Fruit-derived compounds in anticancer targeting

The anticancer effects of fruit-based phytochemicals are influenced by several mechanisms. The modulation of cell signalling pathways related to apoptosis, cell cycle regulation and angiogenesis is possible with these compounds (Atanosov *et al*., 2021). Studies conducted *in silico* have revealed that several fruit phytochemicals interact with crucial proteins involved in the formation of tumours. The presence of resveratrol in grapes has been linked to the activation of tumour suppressor pathways and the suppression of oncogenic signalling pathways such as PI3K/Akt and MAPK (Ko *et al*., 2017; Anwar *et al*., 2023). Also, mangiferin derived from mango displays an affinity for binding proteins involved in regulating apoptosis. Another important class of anticancer phytochemicals is ellagitannins, found in pomegranate and known to interact with enzymes responsible for DNA repair/control of oxidative stress. These molecular interactions are also responsible for suppressing cancer cell proliferation and promoting apoptosis in tumour cells (Zivkovic *et al*., 2024; Mihaylova *et al*., 2025).

5.3 Banana (*Musa* spp.) phytochemicals as lead molecules

One of the world's most popular fruits is banana, which contains a wide range of bioactive compounds that have therapeutic potential. In addition to catecholamines, dopanes, phenolic acids, carotenoids and terpenoid compounds found in banana tissues have antioxidant and anti-inflammatory properties (Sidhu *et al*., 2018). Recent *in silico* studies have evaluated banana-derived phytochemicals as potential inhibitors of viral and bacterial proteins. Dopamine derivatives found in banana peel have shown promising binding affinity toward viral proteases and inflammatory mediators (Senevirathna *et al*., 2024). Additionally, banana carotenoids and terpenoids have demonstrated potential activity against metabolic enzymes involved in diabetes and obesity. These compounds interact with enzyme active sites and regulate metabolic pathways involved in glucose metabolism. The availability of diverse phytochemicals in banana makes it an attractive candidate for natural product drug discovery. Further computational and experimental studies are required to validate the therapeutic potential of banana-derived compounds (Khan *et al*., 2022; Arya *et al*., 2024)

5.4 Case studies of fruit phytochemicals in computational drug discovery

Recent studies into phytochemicals from grape (*V. vinifera*), especially resveratrol, have shown that combining molecular docking, molecular dynamics simulations and network pharmacology is a powerful strategy for discovering compounds with multi-target therapeutic potential. Resveratrol has been widely studied for its interactions with proteins linked to metabolic diseases, cancer and viral infections. In a recent computational study integrating network pharmacology with docking and molecular dynamics approaches, resveratrol was found to associate with key molecular targets such as AKT1 (AKT serine/threonine kinase 1), TNF (tumor necrosis factor) and PPARG (peroxisome proliferator-activated receptor gamma), all of which play significant roles in insulin signalling and inflammatory pathways related to type 2 diabetes (Martínez-Esquivias *et al*., 2025). The stability of these resveratrol-protein complexes was further supported by molecular dynamics simulations, suggesting strong binding efficiency and potential biological relevance. Similarly, another study focused on designing resveratrol derivatives and assessing them through docking analyses against cancer-related enzymes like cyclooxygenase-2 (COX-2), where the modified compounds exhibited improved binding interactions compared to the original molecule (Wu *et al*., 2024). Overall, these studies underline the significance of grape-derived polyphenols as promising multi-target agents and demonstrate the role of computational techniques in speeding up the screening and optimization of bioactive compounds for managing chronic diseases.

Fruit crops such as mulberry (*Morus alba*) and banana (*Musa* spp.) have recently gained attention as sources of bioactive compounds evaluated through multi-target computational approaches. In a comprehensive study, phytochemicals from *M. alba* were analyzed using molecular docking, pharmacokinetic profiling and molecular dynamics simulations against colorectal cancer-associated targets, including EGFR, caspase-3 and caspase-9 (Stany *et al*., 2024). The results indicated that several flavonoids and phenolic compounds exhibited strong binding affinity and stable interactions within the active sites of these proteins, suggesting their role in apoptosis induction and tumour suppression. Similarly, banana-derived compounds, particularly dopamine derivatives and phenolics, have been investigated through docking and network pharmacology approaches, demonstrating their potential to modulate inflammatory cytokines and oxidative stress-related pathways. These studies further highlight the multi-target nature of fruit phytochemicals, which allows them to interact with complex biological networks rather than single molecular targets. The integration of computational techniques in these case studies not only validates the pharmacological relevance of fruit crops but also supports their application as sustainable and effective sources for future drug discovery (Savitri *et al*., 2023).

6. Challenges, limitations and future perspectives

Although *in silico* drug discovery methods have greatly accelerated the identification of potential therapeutic compounds derived from fruit phytochemicals, several scientific and technical limitations still persist. Computational techniques, such as molecular docking and molecular dynamics simulations and pharmacokinetic modelling, offer valuable predictions regarding ligand-protein interactions and drug-like characteristics. However, these forecastsneed to beverified through experimental studies to establish their biological function and clinical significance (Paul *et al*., 2021; Liu *et al*., 2024). The effective advancement of phytochemical based treatments necessitates the combination of computational techniques with experimental studies.

6.1 Limitations of *in silico* predictions

Despite the rapid progress of drug discovery in discovering bioactive phytochemicals, there are still several limitations to computational

predictions. Ligand-protein interactions are estimated by simplified mathematical models, but these models cannot fully account for the dynamic biological environment of living systems (Salimi *et al*., 2022; Alrawashdeh *et al*., 2024). However, some molecular docking algorithms have limitations. Moreover, proteins are frequently depicted as static entities in docking simulations, but their structure undergoes periodic changes during molecular interactions. Virtual screening may not be entirely accurate due to the lack of actual biological activity matching with predicted binding affinities, leading to false-positive results. Furthermore, differences in the scoring algorithms used by docking programs can lead to unpredictable outcomes and might influence the selection and ranking of compounds (Chen, 2015; Guan *et al*., 2018). Additionally, computational ADMET models provide only theoretical estimates of pharmacokinetic behavior and may overlook complex metabolic processes occurring *in vivo*. Thus, while *in silico* methods are useful for initial assessments, they must be complemented with molecular dynamics simulations and experimental validation to guarantee accurate predictions of therapeutic efficacy (Sandeep *et al*., 2023).

6.2 Integration with omics technologies

The integration of omics technologies has significantly enhanced the potential of computational drug discovery in phytochemical research. Modern omics approaches such as genomics, transcriptomics, proteomics and metabolomics allow researchers to analyze complex biological systems and identify key molecular pathways involved in disease progression (Emwas *et al*., 2013; Liu *et al*., 2024). Furthermore, metabolomics approaches employing advanced analytical techniques such as liquid chromatography-mass spectrometry and gas chromatography-mass spectrometry facilitate comprehensive profiling of bioactive compounds present in fruit crops (Paul *et al*., 2021; Pang *et al*., 2023). Additionally, genomic and transcriptomic analyses assist in identifying genes involved in the biosynthesis of pharmacologically significant phytochemicals. Consequently, the integration of omics datasets with ***in silico*** screening platforms can enhance the discovery of novel therapeutic compounds and provide deeper understanding of their mechanisms of action. Additionally, systems biology approaches allow researchers to construct molecular interaction networks that link phytochemicals with disease-related targets. Overall, the combination of omics technologies and computational methods provides a powerful strategy for accelerating natural product-based drug discovery (Chen *et al*., 2015).

6.3 Artificial intelligence and machine learning in natural product based drug discovery

In the exploration of natural products, modern drug discovery has been greatly aided by the use of artificial intelligence and machine learning. The use of these technologies enables the identification of patterns in massive biological and chemical datasets that may not be detectable using traditional computational methods (Vamathevan *et al*., 2019; Paul *et al*., 2021). Furthermore, phytochemical biological activity, toxicity and pharmacokinetics can be predicted using machine learning algorithms on the basis of their molecular structures. Consequently, these AI-driven models allow researchers to rapidly screen thousands of compounds and accurately identify promising drug candidates (Jumper *et al*., 2021). Moreover, deep learning techniques are being increasingly used to analyze complex protein–ligand interaction networks and predict binding affinity with greater precision. Additionally, the integration of AI models with genomic and proteomic databases enables the identification of new therapeutic targets and enhances the effectiveness of natural product research (Askr *et al*., 2023).

6.4 Sustainable utilization of fruit biodiversity

Fruit's biodiversity can be an invaluable resource for discovering new therapeutic compounds, but its sustainable use is crucial for long-term drug discovery efforts. Despite their abundance in the wild and underutilized fruit species, there are still many unique phytochemicals that have not been extensively researched in pharmaceutical research (Mansyah *et al*., 2024). Also, with increasing agricultural intensification and habitat loss these valuable genetic resources are at risk of becoming unavailable. Thus, the protection of fruit crop diversity requires measures such as germplasm conservation, biodiversity management, and sustainable cultivation. Additionally, ethical bioprospecting programs can promote the identification of new bioactive compounds while ensuring the safe and ethical use of natural resources. Additionally, the development of new agricultural technologies and improved crop breeding techniques can lead to an increase in phytochemical content without affecting environmental sustainability (Marappan *et al*., 2025). Consequently, protecting fruit biodiversity not only maintains ecological stability but also fosters a continuous supply of new molecules for drug development and additional uses (Ishfaq *et al*., 2023).

7. Conclusion

The bioactive substances present in fruit crops possess considerable therapeutic importance because of their elevated levels of phytochemicals. Naturally existing substances display a wide range of pharmacological impacts, such as antioxidant, anti-inflammatory, antiviral, anticancer, antimicrobial and neuroprotective effects. The integration of *in silico* drug discovery methods with phytochemical studies has led to much quicker identification of possible drug candidates. Employing computational techniques like molecular docking, molecular simulations, pharmacokinetic modelling, and network pharmacology provides crucial understanding of the interactions between phytochemicals and their target organisms. Phytochemicals derived from fruits have demonstrate defficacy as antiviral agents against various disease targets, including viral proteins, cancer-associated enzymes, metabolic regulators and inflammatory mediators. The multi-target properties of various phytochemicals render them ideally suited for addressing complex diseases that engage several biological pathways. Artificial intelligence, metabolomics and systems biology will enhance the identification of natural drug candidates from fruit crops. The integration of phytochemistry, computational biology and pharmaceutical research creates a robust basis for creating new drugs utilizing the natural resources found in fruits. In the end, ongoing research on fruit phytochemicals and the use of sophisticated computational techniques will significantly aid in creating safe and effective natural pharmaceuticals.

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Data availability

No data was used for the research described in the article.

Ethical statement

Highest possible standards of ethics followed by providing due citations to the works reviewed.

Author's contribution

B. Sindhuja: Writing original draft, Validation, Methodology, Investigation, Conceptualization.

M. Kavino: Writing-review and editing, Validation, Supervision, Resources, Project administration, Methodology, Data curation, Formal analysis.

S. Nakkeeran: Validation, Supervision, Resources, Methodology.

J. Auxcilia, N. Saranya, R. Raghu: Resources, Supervision

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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