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Article

Network Pharmacology Analysis of Lycopene to Identify Its Targets and Biological Effects in Human Tissues

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Abstract: Background: Lycopene exhibits a broad spectrum of biological activities with potential therapeutic applications. Despite its established antioxidant and anti-inflammatory properties, the molecular basis for its pharmacological actions remains incompletely defined. Here we investigated the molecular targets, pharmacodynamic feasibility, and tissue-specific expression of lycopene targets using a network pharmacology approach combined with affinity and protein-protein interaction (PPI) analyses. **Methods:** Lycopene-associated human protein targets were predicted using Swiss target screening platform. Molecular docking was used to estimate binding affinities, and concentration-affinity (CA) ratios were calculated based on physiologically relevant plasma concentrations (75–210 nM). PPI networks of lycopene targets were constructed to identify highly connected targets, and tissue expression analysis was assessed for high-affinity targets using protein-level data from the Human Protein Atlas database. **Results:** Of the 94 predicted targets, 37% were nuclear receptors and 18% were Family A GPCRs. Among the top 15 high-affinity targets, nuclear receptors and GPCRs comprised 40% and 26.7% respectively. Twenty targets had affinities <10 μ M, with six key targets (MAP2K2, SCN2A, SLC6A5, SCN3A, TOP2A, and TRIM24) showing sub micromolar binding. CA ratio analysis identified MAP2K2, SCN2A, and SLC6A5 as pharmacodynamically feasible targets (CA >1). PPI analysis revealed 32 targets with high interaction and 9 with significant network connectivity. Seven targets (TRIM24, GRIN1, NTRK1, FGFR1, NTRK3, CHRN4, and PIK3CD) showed both high affinity and centrality in the interaction network. Expression profiling of submicromolar targets revealed widespread tissue distribution for MAP2K2 and SCN3A, while SCN2A, TOP2A, and TRIM24 showed more restricted expression patterns. **Conclusion:** This integrative analysis identifies a subset of lycopene targets with both high affinity and pharmacological feasibility, particularly MAP2K2, SCN2A, and TRIM24. Lycopene appears to exert its biological effects through modulation of interconnected signalling networks involving nuclear receptors, GPCRs, and ion channels. These findings support the potential of lycopene as a multi-target therapeutic agent and provide a rationale for future experimental and clinical validation.

Keywords: lycopene; network pharmacology; PI3K/AKT; MAPK; oxidative stress; inflammation; molecular docking; systems biology

1. Introduction

Lycopene, a naturally occurring lipophilic dietary carotenoid found predominantly in tomatoes and other red coloured fruits/vegetables, has been extensively studied for its health benefits. Lycopene concentrations per 100 grams for some common sources are as follows; guava: 5,204 micrograms (mcg), cooked tomatoes: 3,041 mcg, watermelon: 4,532 mcg, pink grapefruit: 1,419 mcg, papaya: 1,828 mcg, red bell peppers (cooked): 484 mcg, persimmon: 159 mcg, asparagus (cooked): 30 mcg and red cabbage: 20 mcg. It's important to note that lycopene concentrations can vary based on factors such as ripeness, variety, and growing conditions.[1–3] The global lycopene market is valued

at approximately Euro 160 million in 2023 and is projected to grow at a compound annual growth rate (CAGR) of 5.1% from 2024 to 2030.[4,5] The average daily lycopene intake ranges from 5 to 11 mg per capita.[4,5] Epidemiological studies have associated high dietary intake of lycopene with reduced risks of chronic diseases such as cardiovascular ailments and certain cancers. These observations have spurred extensive research into the bioactive properties of lycopene, particularly its antioxidant and anti-inflammatory effects.[6,7]

Lycopene was first isolated from the berries of *Tamus communis* by a chemist Frederik Anthony Hartsen in 1873.[8] Subsequently, in 1875, it was extracted from tomatoes by a botanist Alexis Millardet as a crude crystalline mixture, who named it as solanorubin. It wasn't until 1903 that chemist Carl A. Schunck identified this red pigment as distinct from other carotenoids and named it "lycopine" probably deriving the term from the tomato's botanical name, *Lycopersicon esculentum*. [9,10] It isn't clear how in colloquial use lycopine became lycopene, which tends to be the current nomenclature. Lycopene (PubChem ID 446925; MF: C₄₀H₅₆, MW: 536.9 g/mol) is a carotenoid characterized by its linear, acyclic structure composed of 40 carbon atoms forming a series of 13 double bonds, 11 of which are conjugated.[11,12] This extensive conjugated system imparts lycopene with its deep red colour and potent antioxidant properties.[11,12] This conjugated system allows lycopene to absorb light in the blue and green regions of the visible spectrum, with absorption maxima around 505 nm. As a result, the remaining unabsorbed light is rich in red wavelengths, which are reflected, giving lycopene its characteristic red colour. The number of conjugated double bonds in a molecule directly influences its colour (a greater number of these bonds shifts absorption toward longer wavelengths, resulting in the reflection of colours like red). Unlike many other carotenoids, such as β -carotene, which possess cyclic end groups (rings) at both ends of their structures, lycopene lacks these terminal rings, resulting in its open-chain configuration.[11–13] Additionally, lycopene does not exhibit pro-vitamin A activity, distinguishing it functionally from carotenoids like β -carotene that can be converted into vitamin A in the human body.

Lycopene exhibits distinct pharmacokinetic properties in humans. Upon ingestion, lycopene is incorporated into lipid micelles in the small intestine, facilitated by dietary fats and bile salts. Absorption occurs primarily via passive diffusion and is mediated by scavenger receptor class B type 1 (SR-B1).[14,15] Once absorbed, lycopene is transported through the lymphatic system within chylomicrons and subsequently distributed to various tissues, with notable accumulation in the liver, adrenal glands, and testes.[16,17] The compound undergoes extensive isomerization, predominantly converting from the all-trans form to cis-isomers, which are more bioavailable and preferentially accumulate in tissues.[16] Metabolism involves oxidative cleavage by enzymes such as β -carotene oxygenase 2 (BCO2), leading to the formation of polar metabolites excreted via urine. Pharmacokinetic studies have reported following single dose administration (10 to 30 mg) in healthy human adult males, a time to reach maximum plasma concentration (0.08–0.21 μ M) (Tmax) ranging from 15 to 33 hours post-ingestion, with a half-life varying between 28 to 62 hours and volume of distribution varying from 250 to 800 litres, indicating prolonged retention in the body.[16,18] These parameters can be influenced by factors including the food matrix, presence of dietary fats, and individual variations in metabolism. Understanding these pharmacokinetic characteristics is essential for optimizing lycopene's therapeutic applications and determining appropriate dosing regimens.

Lycopene has gained significant attention for its broad spectrum of pharmacological activities. Its principal mechanisms of action include potent antioxidant, anti-inflammatory, and anti-proliferative effects, which collectively contribute to its therapeutic potential across a range of human diseases.[7,19–22] As a strong antioxidant, lycopene efficiently scavenges reactive oxygen species (ROS), thereby protecting cells from oxidative damage, a critical factor in the pathogenesis of cardiovascular diseases, cancers, and neurodegenerative disorders.[7,19,20] Lycopene modulates inflammatory responses by inhibiting pro-inflammatory cytokines and promoting negative feedback mechanisms that suppress chronic inflammation. This anti-inflammatory effect plays a vital role in conditions such as cardiovascular disease, where lycopene improves vascular function and reduces

In this study, we employed network pharmacology methodologies to systematically explore the molecular mechanisms and biological targets of lycopene in humans. By integrating data from open-access databases, we identified lycopene-associated proteins and constructed a PPI network to discern critical nodes and pathways. Furthermore, molecular docking analyses were performed to assess the binding affinities between lycopene and its potential targets, providing insights into the compound's pharmacological interactions. This comprehensive approach aims to bridge the gap between observational studies and mechanistic insights, thereby advancing our understanding of lycopene's therapeutic potential and informing future research directions.

Chemical structure of lycopene (PubChem ID 446925) was identified in PubChem database and its SMILES ID

(CC=(CCC/C(=C/C=C/C(=C/C=C/C(=C/C=C/C(=C/C=C/C(/C=C/C=C(/C=C/C=C(/CCC=C(C)C)\C)\C)\C)/C)/C)/C) was input into the SwissTargetPrediction web-based tool (<http://www.swisstargetprediction.ch/>) with Homo sapiens species section to identify all potential targets of lycopene. The target class of the lycopene targets identified were assessed as percent of the total targets for all the targets and as well as top 15 targets. The lycopene targets identified were cross checked for validity in the UniPort database (<https://www.uniprot.org/>) and their AlphaFold (if available) 3D structure was downloaded in PDB format. For the targets where the AlphaFold was not available, homology modelling as reported before was used to generate a 3D structure.[36,37] The affinity values of lycopene to its identified targets were assessed using AutoDock vina 1.2.0 as reported before for other ligand-receptor combinations.[38,39]

To assess the targetability potential of all identified targets by lycopene, the concentration affinity ratio (CA ratio) for each of the targets was calculated as described before.[36] The following plasma concentration range of lycopene, 75

170 and 210 nM was used for the CA ratio assessment based on the lycopene dose range of 10, 30 and 90 mg/day and its volume of distribution of 520 litres.[16] The CA ratio of lycopene to all its identified targets is presented as a heat map.

To assess the protein-protein interactions between the lycopene targets, protein structure of the targets (PDB files) was imported into Chimera software in pairs and the number of hydrogen bonds

(H-bond) formed between each pair of targets at 10 Å distance was evaluated. The data of these interactions was inputted into the Microsoft Excel sheet and a heat map was generated using the conditional formatting colour scale tool to identify major networks. The networks of the lycopene targets were categorised into the following two groups; 1) high interacting networks and 2) significantly interacting networks based on at least ten pairs of targets showing >8000 H-bond between them using the quartile logic. If a minimum of ten pairs of targets showed >15000 H-bond between them, then the target was categorised to have significantly interacting networks. A Venn diagram was plotted using the list of 1) all targets, 2) targets with high interacting networks and 3) targets with significantly interacting networks to illustrate the logical relationships between these three datasets.

All the identified targets of lycopene with affinity values <1 μM were evaluated for their tissue specific protein expression using the Human Protein Atlas (<https://www.proteinatlas.org>) database.[36,40] Of the six high affinity targets we could analyse only five as protein expression data of SLC6A5 wasn't available. The tissue specific protein expression data of the remaining five high affinity lycopene targets (MAP2K2, SCN2A, SCN3A, TOP2A and TRIM24) were plotted using Venn diagram to assess the logical relationships between the expression pattern of the targets and to identify if any specific tissue type is of preference for lycopene pharmacological effects.

3. Results

The target prediction screening of lycopene showed 94 possible targets with affinities varying from 57 nM to 14 mM (Figure 1). A significant proportion of lycopene targets were nuclear receptors (37%) followed by Family A G protein coupled receptors (GPCR 18%), while the rest of the target categories ranged from 2-8% (Figure 1). When only the top 15 targets of the lycopene were assessed, six different target classes were identified, of which 40% were nuclear receptors followed by GPCR (26.7%), ion channels (13%), phosphatases (6.7%), secreted protein (6.7%) and ligand gated ion channels (6.7%). Twenty targets of lycopene were observed to have affinity values <10 μM and of these twenty targets the following targets showed affinity values <1 μM; MAP2K2, SCN2A, SLC6A5, SCN3A, TOP2A and TRIM24.

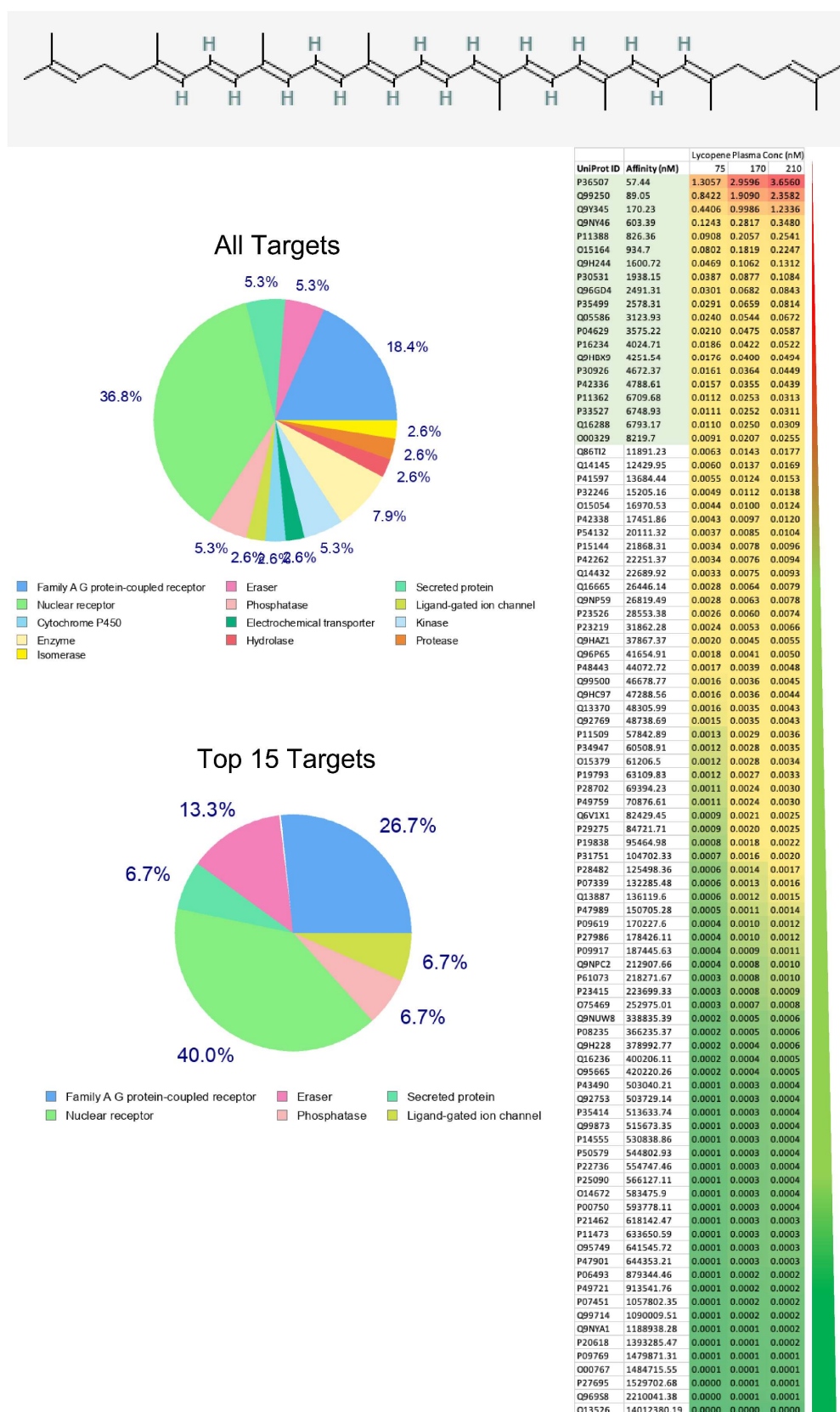


Figure 1. The chemical structure of lycopene to outline its linear nature is shown. The target class of all and top 15 lycopene targets are shown as pie chart along with the relative percent of each of the target categories. The heat map shows the affinity and concentration-affinity (CA) ratio values (for plasma concentration of lycopene of 75, 170 and 210 nM) for each of the lycopene targets. The lycopene targets are represented by their UniProt

ID. The lycopene targets highlighted in green are high affinity targets all will affinity values $<10\mu\text{M}$. The heat map scale shown is from high (red) to low (green) CA ratio.

To assess the targetability of the lycopene targets, we looked at concentration-affinity (CA) ratios at the following plasma concentration of lycopene 75, 170, 210 nM which was based on the dose rate of 10-90 mg/day in humans. The CA ratio analysis indicated the feasibility of targeting the following three targets MAP2K2, SCN2A and SLC6A5 as their CA ratio was >1 , while the rest of the lycopene target showed CA ratio of <0.1 , suggesting the affinities values of lycopene to these targets was ten folds greater than plasma concentrations of lycopene.

The protein-protein interaction (PPI) analysis of all lycopene targets indicated 32 high interaction and 9 significant interaction targets (Figure 2). Of the 32 high interaction targets 5 (TRIM24, GRIN1, NTRK1, FGFR1 and NTRK3) showed affinity values to lycopene under $10\mu\text{M}$, while among the 9 significant interaction targets only two (CHRNA4 and PIK3CD) showed affinity values to lycopene under $10\mu\text{M}$. Although the CA ratios of these lycopene targets with affinity values $<10\mu\text{M}$ ranged from 0.01 to 0.03. Most lycopene targets in addition to showing low affinity values had negligible PPI (<10 hydrogen bonds), suggesting these targets are not of relevance to the pharmacological effects of lycopene or may be indirectly regulated. Based on the PPI and affinity values we observe the three categories of lycopene targets, i.e., 1) targets with high affinity values ($<10\mu\text{M}$; MAP2K2, SCN2A, SLC6A5, SCN3A, TOP2A, TRIM24, P2RY12, SLC6A1, AURKB, SCN4A, GRIN1, NTRK1, PDGFRA, RXFP1, CHRNA4, PIK3CA, FGFR1, ABCC1, NTRK3 and PIK3CD), 2) targets with high network interactions (TRIM24, GRIN1, NTRK1, CHRNA4, FGFR1, NTRK3, PIK3CD, CLK4, RXRG, CYP2A6, GRK5, RXRA, RXRB, CLK1, NFKB1, MAPK1, PDGFRB, PIK3R1, CXCR4, GLRA1, NR1I2, NR3C2, NFE2L2, NAMPT, PRMT1, METAP2, NR4A1, ADAM10, VDR, HSD17B10, SPHK1 and APEX1) and 3) targets with both high affinity values and network interactions (TRIM24, GRIN1, NTRK1, FGFR1, NTRK3, CHRNA4 and PIK3CD) (Figure 2).

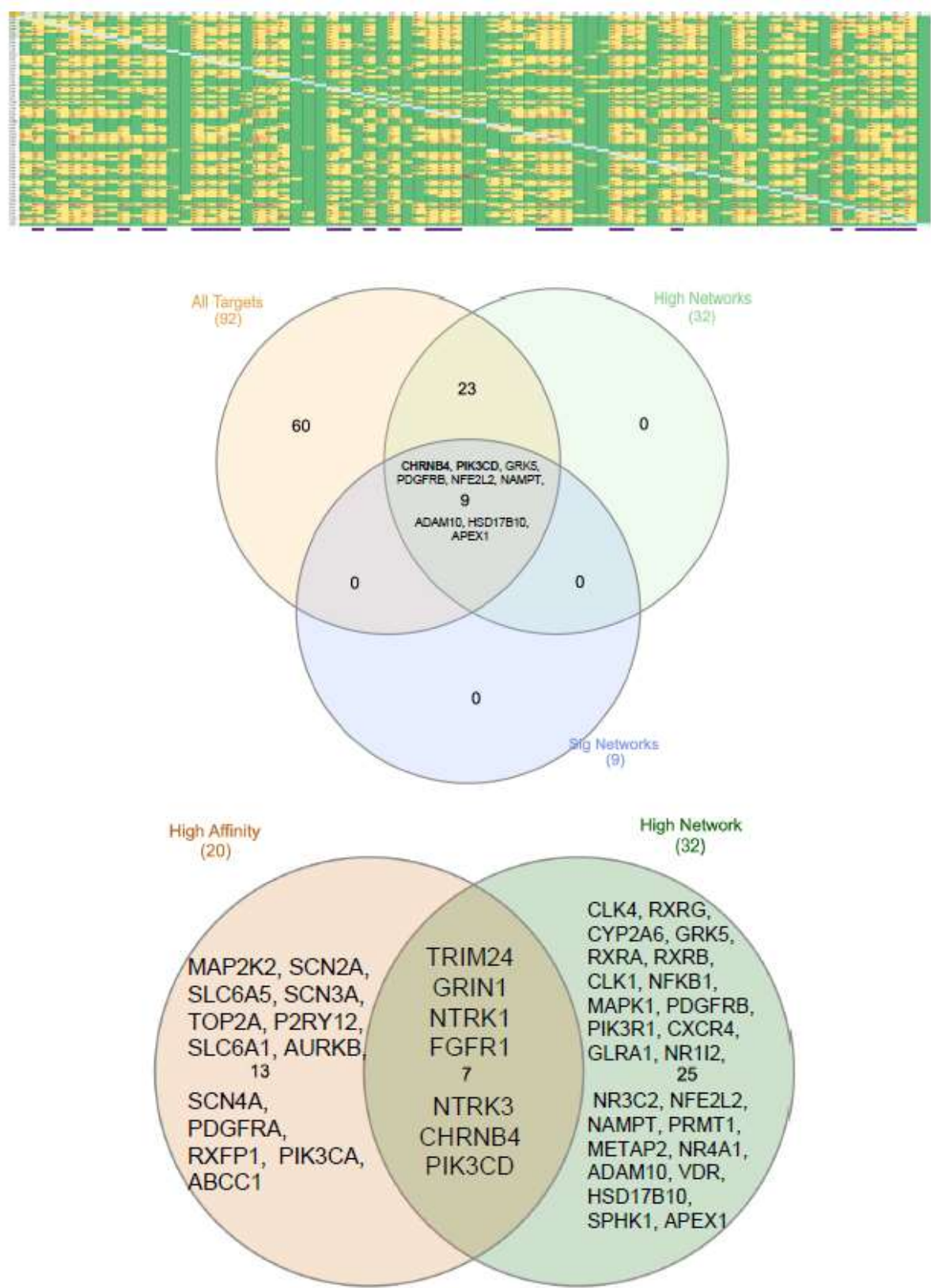
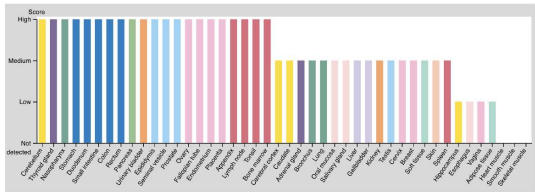
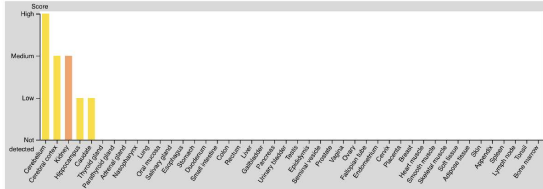


Figure 2. Heat map of the protein-protein interaction networks of all lycopene targets, based on the number of hydrogen bonds formed between a pair of targets at 10 Armstrong distance. Venn diagram in the middle shows the logical relationships between all, high (at least ten pairs of targets showing >8000 H-bond between them) and significant (a minimum of ten pairs of targets showed >15000 H-bond between them) network targets of lycopene. The Venn diagram below shows the logical relationships between high affinity and high network targets of lycopene. The three major categories of lycopene targets are shown i.e., 1) high affinity targets (orange), 2) high network targets (green) and 3) targets with high affinity and networks (olive).

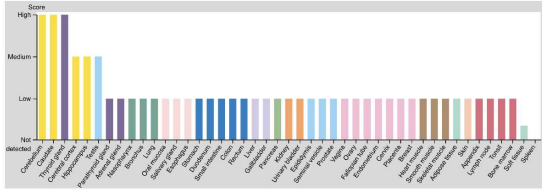
Tissue Expression of MAP2K2 protein



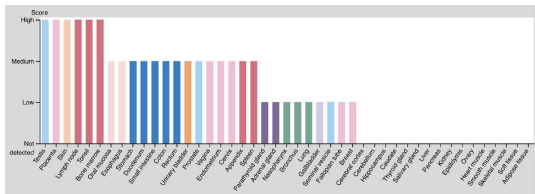
Tissue Expression of SCN2A protein



Tissue Expression of SCN3A protein



Tissue Expression of TOP2A protein



Tissue Expression of TRIM24 protein

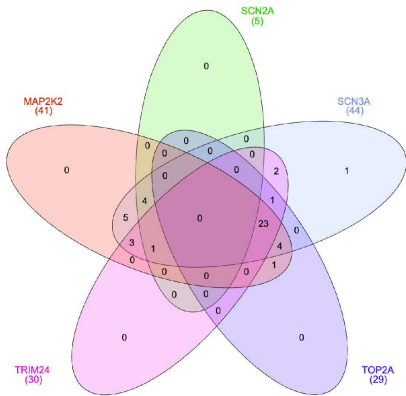
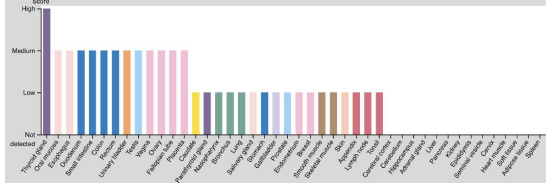


Figure 3. Tissue specific protein expression of the top five high affinity targets (MAP2K2, SCN2A, SCN3A, TOP2A and TRIM24) of lycopene in humans. Expression of MAP2K2, SCN2A, SCN3A, TOP2A and TRIM24 was observed in 41, 5, 44, 29 and 30 different tissues. The Venn diagram shows the synergistic relationship between the tissues expressing top five high affinity targets of lycopene. MAP2K2, SCN3A, TOP2A and TRIM24 were collectively expressed in 23 different tissues, while SCN3A was the only lycopene target expressed in heart muscle.

For the expression analysis of the lycopene targets in human tissues, we only looked at high affinity targets with affinity values $<1\mu\text{M}$ as these targets are most likely to be pharmacodynamically preferred. Hence the following targets MAP2K2, SCN2A, SLC6A5, SCN3A, TOP2A and TRIM24 were assessed for their tissue specific expression pattern. As we selectively looked at protein expression pattern, SLC6A5 was excluded as its protein expression data is still pending normal tissue annotation. Moreover, its RNA expression data is limited to the following tissues, lung, spinal cord, cerebellum, pituitary gland, testis and cerebral cortex in humans with the number of transcripts per million (nTPM) value <1 . The remaining 5 lycopene targets, except SCN2A (expressed in 5 tissue types) showed extensive tissue expression with MAP2K2 and SCN3A being widely expressed. MAP2K2, SCN3A, TOP2A and TRIM24 were collectively expressed in 23 different tissues. MAP2K2, SCN3A, TOP2A and TRIM24 were all expressed in seminal vesicle, bone marrow, adrenal gland and cervix. SCN3A, TOP2A and TRIM24 were collectively expressed in parathyroid gland only. SCN3A and TRIM24 were collectively expressed in smooth and skeletal muscles. MAP2K2 and TOP2A were collectively expressed in spleen only. MAP2K2, SCN2A, SCN3A and TRIM24 were collectively expressed in caudate nucleus only. MAP2K2, SCN3A and TRIM24 were collectively expressed in thyroid gland, ovary and salivary gland. MAP2K2 and SCN3A were collectively expressed in pancreas, epididymis, liver, soft and adipose tissue. MAP2K2, SCN2A and SCN3A were collectively expressed in cerebellum, cerebral cortex, kidney and hippocampus. SCN3A was exclusively expressed in heart muscle. High expression of MAP2K2 protein was observed in 21 different tissues, while high expression of SCN2A (cerebellum), SCN3A (cerebellum, caudate nucleus and thyroid gland), TOP2A (testis, placenta, skin, lymph node, tonsil and bone marrow) and TRIM24 (thyroid gland) was observed only in one or few tissues.

4. Discussion

This study provides a comprehensive network pharmacology analysis of lycopene, revealing its multi-target interactions and potential pharmacodynamic actions in human tissues. The in-silico target prediction identified 94 candidate targets, with affinity values ranging from 57 nM to 14 mM, highlighting the broad spectrum of lycopene's molecular mechanisms.[20,30,41,42] This is particularly not surprising considering the broad spectrum of health benefits reported following lycopene use.[16,21,43,44] Notably, nuclear receptors constituted the largest proportion (37%) of target classes, consistent with previous findings that carotenoids often modulate gene expression via nuclear receptor pathways.[45–47] GPCRs represented the second-largest category (18%), indicating lycopene's potential to modulate signalling at the membrane receptor level as well. Focusing on the top 15 targets of lycopene, six distinct target classes were identified, dominated again by nuclear receptors (40%) and GPCRs (26.7%), which is again consistent with prior reports indicating lycopene's ability to modulate transcriptional and signalling pathways involved in inflammation, metabolism, and cellular proliferation.[6,34,41]

Among the 20 targets with sub-10 μM affinities, six targets (MAP2K2, SCN2A, SLC6A5, SCN3A, TOP2A, and TRIM24) exhibited high-affinity binding ($<1\mu\text{M}$), suggesting these targets are most likely to be pharmacologically modulated at physiological concentrations of lycopene. While lycopene is known for its weak direct activity at most proteins due to its hydrophobic nature and limited aqueous solubility,[48,49] our concentration-affinity (CA) ratio analysis provided critical pharmacodynamic context. Only three targets (MAP2K2, SCN2A, and SLC6A5) showed CA ratios >1 at reported human plasma concentrations (75–210 nM), suggesting these are the most pharmacologically viable targets under physiological conditions. While compounds with CA ratios >1 are more likely to exert biological effects at attainable plasma levels, considering previous studies indicating that lycopene exerts biological activity at nanomolar concentrations,[50–52] particularly within membrane-rich environments or lipid rafts where its accumulation is higher,[53,54] it is likely that other lycopene targets with CA ratios <1 can potentially be involved in its pharmacodynamic effects.

Protein-protein interaction network analysis further identified a subset of targets with significant biological relevance. We identified 32 high-interaction and 9 significant-interaction proteins, with some of these targets (TRIM24, GRIN1, NTRK1, FGFR1, and NTRK3) exhibiting binding affinities below 10 μ M. Although their CA ratios remained low (<0.03), these targets may act as secondary effectors or be relevant in tissues with higher lycopene accumulation, such as the prostate, liver, and adrenal glands.[16,55] TRIM24, GRIN1, NTRK1, FGFR1, NTRK3, CHRNA4, and PIK3CD are key proteins with diverse biological roles, many of which are relevant to disease pathogenesis and potential pharmacological targeting.[56–58] TRIM24 is a transcriptional co-regulator that influences nuclear receptor signalling and chromatin remodelling, playing critical roles in cell proliferation and apoptosis and hence it is implicated in cancer, particularly breast and liver malignancies.[59,60] GRIN1 encodes a core subunit of NMDA receptors, essential for calcium ion influx during synaptic transmission. It is central to learning, memory, and neural development, and its dysregulation is associated with neurodegenerative diseases due to excitotoxicity.[61,62] Alterations in NTRK1 is linked to various cancers and sensory disorders, while NTRK3 is associated with breast carcinoma and congenital fibrosarcoma.[63,64] FGFR1, by mediating pathways involved in growth, angiogenesis, and tissue repair contributes to developmental syndromes and several cancers while CHRNA4 is critical for synaptic transmission in the nervous system and is implicated in neurological conditions such as epilepsy, schizophrenia, and nicotine dependence.[65–67] PIK3CD is predominantly expressed in immune cells and regulates pathways central to immune function, and its mutations are associated with primary immunodeficiencies like Activated PI3K-Delta Syndrome.[68] Hence PIK3CD is a target of interest in autoimmunity and cancer therapy. These novel observations in our study on the diverse pathophysiological role of lycopene targets identified is consistent with several clinical investigations and reports on potential use of lycopene use in healthcare.[21,69,70]

Expression profiling of the highest affinity targets provided further insight into tissue-specific pharmacodynamics of lycopene. Except for SLC6A5, whose protein expression data remains limited, the remaining high-affinity targets showed expression in a range of tissues. MAP2K2, SCN3A, TOP2A, and TRIM24 are functionally involved in oncogenic signalling, neuronal excitability, and DNA repair, offering diverse but interconnected avenues for pharmacological intervention. Particularly, MAP2K2, SCN3A, TOP2A, and TRIM24 were co-expressed in reproductive and endocrine tissues (seminal vesicle, adrenal gland, and cervix). These results are in line with past transcriptomic studies that observed upregulation of lycopene-responsive genes in prostate and mammary tissues.[54,71,72] MAP2K2 is a critical component of the MAPK/ERK signalling pathway, which regulates cell proliferation, differentiation, and survival. Aberrant activation of MAP2K2 has been linked to various cancers, particularly melanoma and colorectal cancer, making it a validated target for anti-cancer therapies.[73,74] Pharmacological inhibition of MAP2K2 has shown potential in overcoming resistance to upstream oncogenes such as BRAF and RAS and it remains to be tested if lycopene can have synergistic effects with these established MAP2K2 inhibitors to achieve optimal pharmacodynamic outcomes while minimising any potential adverse effects. Interestingly, SCN3A, a voltage-gated sodium channel, showed unique expression in the heart, pointing to possible roles in cardiac excitability supporting prior studies that suggested cardiovascular benefits of lycopene via electrophysiological and anti-inflammatory mechanisms.[75] SCN3A is predominantly expressed in the central nervous system, where it is essential for the initiation and propagation of action potentials in neurons. Dysregulation or mutations in SCN3A are associated with neurological disorders including epilepsy, developmental and epileptic encephalopathies, and cognitive impairments. SCN3A represents a target for anticonvulsant development and therapies aimed at modulating neuronal excitability.[76,77] Based on these there seems to be merit in assessing the potential of lycopene in connecting the heart-brain axis via SCN3A targeting. TOP2A, and TRIM24 have a vital role in DNA replication, transcription, and chromosome segregation and are well-established targets in cancer chemotherapy especially in breast, prostate, and liver cancers.[78,79] Our report of high

affinity targeting of TOP2A, and TRIM24 opens avenues for synergistically improving the pharmacodynamics of currently used chemotherapeutics (etoposide and doxorubicin) with lycopene.

Collectively, our findings suggest MAP2K2 and SCN2A as the most pharmacodynamically plausible direct targets of lycopene in humans. Their strong affinity, favourable CA ratios, and wide tissue expression profiles make these targets to have a foundational role in mediating lycopene's pharmacological actions. Additional targets such as TRIM24, TOP2A, and NTRK family members, while displaying lower CA ratios, may contribute to lycopene's broader systems-level impact, particularly in the context of inflammation, cancer biology, and neuroprotection. These multi-target interactions are consistent with lycopene's observed pleiotropic benefits in clinical and preclinical models.[7,30,36,44,80]

In conclusion, our study advances the mechanistic understanding of lycopene pharmacology by integrating affinity profiling, network analysis, and expression mapping. While the hydrophobicity and relatively low systemic concentrations of lycopene pose challenges for classical drug-likeness, its selective interaction with key signalling and nuclear proteins highlights its potential as a nutraceutical agent with systems-level effects which merits advancing its use for therapeutic applications. Future studies should aim to validate these interactions in functional cellular assays and assess tissue-specific accumulation patterns to better delineate lycopene's therapeutic potential.

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Declaration of interest statement: none.

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