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REVIEW

Properties of Approved Antitumour Chinese Herbal Medicines: Integrating Evidence and Tradition

Linlin Qi[1,*], Shushu Qian[2,*], Ling Wang[1,*], Zhixu Liu[1], Jiaxin Jiang[1], Chunmei Liu[3], Yang Pan[3], Bo Wang[4], Xuan Han[1,5], Jing Chen[1]

[1]National Key Laboratory of Technologies for Chinese Medicine Pharmaceutical Process Control and Intelligent Manufacture, Nanjing University of Chinese Medicine, Nanjing, People's Republic of China; [2]Department of Rehabilitation Medicine, Center for Rehabilitation Medicine, Rehabilitation & Sports Medicine Research Institute of Zhejiang Province, Zhejiang Provincial People's Hospital, Affiliated People's Hospital, Hangzhou Medical College, Hangzhou, People's Republic of China; [3]College of Pharmacy, Nanjing University of Chinese Medicine, Nanjing, People's Republic of China; [4]Department of Biopharmacy, China Pharmaceutical University, Nanjing, People's Republic of China; [5]School of Integrated Medicine, Nanjing University of Chinese Medicine, Nanjing, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xuan Han; Jing Chen, Email hanxuan@njucm.edu.cn; jingchen3236@njucm.edu.cn

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Abstract: The properties and meridian affinities of Chinese herbal medicine are closely associated with their therapeutic efficacy. This review focuses on approved antitumour Chinese medicines listed in the Pharmacopoeia of the People's Republic of China (2020 Edition, Volume I), highlighting their key components. Statistical methods were used to analyse the properties, flavours and channel tropisms of antitumour traditional Chinese medicine (TCM), including both proprietary formulations and commercially available individual herbs. Distinctive patterns were identified by comparing herb profiles with contemporary experimental studies on antitumour TCM. Analysis revealed that bitter-cold herbs represented the highest proportion of antitumour TCM, with most showing tropism towards the liver channel. These findings provide a reference framework for antitumour drug development, indicating that bitter-cold herbs merit priority as candidate ingredients.

Keywords: antitumour traditional chinese medicine, properties, flavours, channel tropism

Introduction

Cancer poses a major threat to global public health, with incidence and mortality rates continuing to rise. According to the World Health Organization, over ten million new cancer cases are diagnosed worldwide annually, and this burden is expected to grow substantially in coming decades. (https://www.who.int/srilanka/news/detail/05-02-2025-world-cancer-day-2025–the-world-cancer-day-theme-2025-2027-united-by-unique–places-people-at-the-centre-of-care-and-explores-new-ways-of-making-a-difference) Current mainstream therapies include chemotherapy, targeted therapy and immunotherapy. Chemotherapy (eg platinum-based agents and taxanes) eradicates cancer cells by disrupting DNA replication or cell division, targeted therapy (eg small-molecule inhibitors and monoclonal antibodies) selectively inhibits tumour-specific genetic mutations or signalling pathways, and immunotherapy (eg PD-1/PD-L1 inhibitors) enhances immune recognition and elimination of tumours. However, these interventions all face considerable limitations, including frequent resistance requiring regimen adjustments, severe toxicities across modalities, prohibitive financial costs and limited accessibility.

The theory of Chinese medicinal herbs emphasises holistic regulation and syndrome differentiation, offering novel therapeutic opportunities in oncology through its extensive herbal pharmacopoeia and compound formulations. Extensive laboratory and clinical studies have consistently shown that numerous medicinal botanicals and their bioactive phytochemicals exert potent antitumour effects, including but not limited to inhibition of neoplastic proliferation, induction of

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programmed cell death, reversal of multidrug resistance phenotypes and enhancement of host immunity. This growing pharmacological validation has accelerated the development of standardised antitumour proprietary formulations, exemplified by Bruceae Fructus capsules [*Brucea javanica* (L). Merr.], Cinobufagin capsules (Huachansu) and Xiaoaiping tablets, although systematic documentation of their clinical utilisation remains limited.

The theory of medicinal properties forms a cornerstone of traditional Chinese medicine (TCM) pharmacology, formally recorded in the Divine Farmer's Materia Medica (Shennong Bencao Jing) during the Han Dynasty, which states, "Medicinals manifest five flavours (sour, bitter, sweet, pungent and salty) and four thermal properties (cold, hot, warm and cool)". Subsequent works, including the Shuyong Bencao Yaoxing (Liu Song Dynasty), Yaoxing Lun (Tang Dynasty) and Yaoxing Bencao (Tang Dynasty), expanded this pharmacological framework. This systematic paradigm, grounded in classical epistemological principles, such as inferring internal dynamics from external manifestations and analogical reasoning, categorises herb-derived therapeutic actions through three interrelated dimensions. Regarding the Four Properties (si qi), thermal characteristics modulate yin–yang imbalances and cold/heat pathologies. For the five flavours (wu wei), taste profiles dictate bioactivities: pungent agents induce diaphoresis and open meridians, sweet substances tonify qi and blood while harmonising formulations, sour herbs exert astringent effects, bitter herbs clear internal heat and dry dampness through purgative actions and salty compounds soften hardness through downwards-draining properties. The concept of meridian tropism in TCM originates from *The Yellow Emperor's Inner Classic*; Channel Tropism (gui jing) denotes selective affinity for specific zang-fu organ systems and mediates therapeutic outcomes by regulating qi–blood dynamics within corresponding meridians. Rooted in zang-fu and meridian theory, this framework was established through systematic clinical observation of therapeutic outcomes across defined pathological states. Collectively, this tripartite system underpins syndrome differentiation–based treatments in TCM, enabling precise prediction of herb efficacy and rational clinical application by integrating physiochemical attributes with philosophical constructs. Interpreting these parameters synergistically remains essential for guiding herb compatibility and optimising therapeutic regimens.

This review systematically catalogues proprietary antitumour formulations marketed in recent years and classical herbal prescriptions with documented anticancer efficacy, sourcing pharmacological data from the "Properties, Flavors and Channel Tropism" section of the Pharmacopoeia of the People's Republic of China (2020 Edition, Volume I) and the 2022 National Blue Book of TCM Supervision. Our search identified 110 distinct therapeutic entities (74 proprietary preparations and 36 classical formulas), encompassing 251 unique botanical materials. Phytochemical profiling delineated their predominant active constituents, accompanied by rigorous analysis of thermal properties (cold/heat attributes) and meridian affinities. Integration with contemporary anticancer research revealed mechanistic correlations between these pharmacodynamic parameters and antitumour activity. Quantitative assessment showed a predominance of bitter-flavoured botanicals (118/251, 47.0%), followed by sweet (104, 41.4%), pungent (85, 33.9%), salty (21, 8.4%) and sour (13, 5.2%) variants. This phytochemical hierarchy suggests that bitter compounds confer distinctive therapeutic advantages in oncology, warranting further pharmacological exploration to provide an evidence-based framework for developing antitumour herbal agents.

Bitter Medicinals

Bitter medicinals represent a core pharmacodynamic category in TCM, distinguished by heat-clearing and fire-purging actions, dampness-drying effects and the capacity to stabilise yin.[1] These attributes underpin their clinical application in febrile and inflammatory disorders, dampness syndromes and yin deficiency with hyperactive yang. Numerous proprietary formulations derived from bitter herbs have shown notable efficacy in oncological therapy. Among the 118 bitter botanicals identified from 251 antitumour herbs in our survey, cold-natured types predominated (55 species, 46.4%), followed by warm-natured (22 species, 18.6%), cool-natured (11 species, 11.0%) and neutral-natured (3 species, 2.5%) herbs (Figure 1).

Bitter-Cold Medicinals

Bitter-cold medicinals, defined by bitter flavour and cold thermal properties, primarily exert heat-clearing, fire-purging and detoxifying effects and are widely applied in treating dampness–heat toxin syndromes. Owing to their strong heat-

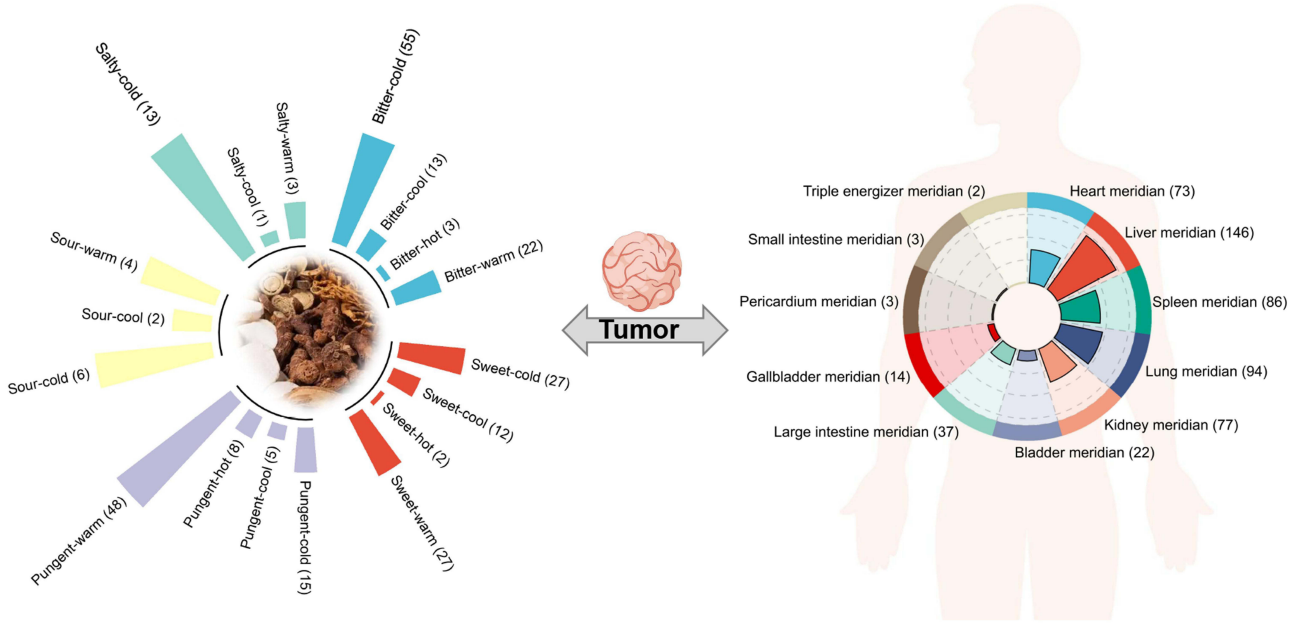

Figure 1 Quantitative analysis and Meridian tropism of the five flavours in antitumour medicinal plants. Left panel: distribution of herbs categorised by the "five flavours" (outer ring) and their corresponding "four properties" (inner bars), highlighting the predominance of bitter-cold and pungent-warm medicinals. Right panel: meridian tropism frequencies, showing that the liver meridian is the most frequently targeted channel, followed by the lung and spleen meridians.

clearing capacity, cautious use is necessary to prevent impairment of yang qi. *Coptis chinensis* Franch. exemplifies this category, displaying broad meridian tropism involving the heart, spleen, stomach, liver, gallbladder and large intestine, with clearing damp-heat and eliminating fire toxins as its principal actions. These medicinals also regulate ministerial fire to preserve yin; for example, *Phellodendri Chinensis* preferentially targets the lower energiser and is effective against yin-deficiency fire syndromes and toxic sores. In contrast, *Picrorhiza scrophulariiflora* Pennell ex Benth. exhibits predominant hepatic tropism, with marked efficacy in clearing deficiency heat associated with blood-deficiency fever.

Phytochemical constituents of bitter-cold herbs exert multifaceted antitumour effects via mechanisms including programmed cell death induction, aberrant proliferation suppression, metastasis inhibition, angiogenesis blockade, immune surveillance potentiation and multidrug resistance reversal. These bioactive compounds regulate critical oncogenic processes, including cell-cycle progression, telomerase activity and signal transduction cascades, culminating in broad anticancer efficacy.[2–6] For instance, paeoniflorin, a major component of *Paeoniae Radix Rubra*, induces tumour cell apoptosis through the NF-κB, STAT3 and p53/14-3-3 signalling pathways, thereby inhibiting tumour proliferation while preventing metastasis and invasion.[7] As a bitter and cold herb, *Rhus verniciflua* is rich in characteristic bitter constituents (eg *Rhus verniciflua* bitter substance, *Rhus verniciflua* bitter alcohol and *Rhus verniciflua* glycoside). Additionally, raven's gall bitter substance D inhibits HIF-1α–mediated glucose metabolism by blocking the ICAT/β-catenin pathway, thereby inhibiting liver cancer cell growth in vitro and in xenograft models.[8]

Bitter-Cool Medicinals

Bitter-cool medicinals, characterised by their bitter flavour and cool thermal nature, are mainly employed in TCM for heat-clearing, detoxifying and blood-cooling purposes. In the present review, 11 bitter-cool herbs were identified, accounting for 11% of all herbs. Several clinically validated antitumour formulations incorporate these agents as key components, including Cinobufacini, Bo'erning and Fushenkang capsules. Cinobufacini, derived from the skin of *Bufo gargarizans* Cantor, exhibits antitumour activity primarily through bufotoxins and indole alkaloids. Its mechanism involves selective elevation of intracellular reactive oxygen species (ROS) in cancer cells, leading to oxidative DNA damage, replication stress, ATM/ATR–Chk signalling activation, G_2/M cell-cycle arrest and subsequent mitochondrial apoptosis via caspase-3 activation. Concurrent inhibition of the PI3K/Akt/mTOR and STAT3 pathways further suppresses tumour proliferation and invasion.[9,10] Another representative bitter-cool medicinal, *Ligustrum lucidum* Ait., contains

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iridoid glycosides and triterpenic acids as major active components. Its antitumour effects are primarily mediated by promoting DNA demethylation of the tumour suppressor gene *PTEN*, thereby inhibiting PI3K/Akt signalling, regulating B-cell lymphoma-2 (Bcl-2) expression, activating mitochondrial apoptosis and inducing cell-cycle arrest to suppress tumour cell proliferation.[11]

Bitter-Warm Medicinals

Bitter-warm medicinals constitute a distinct category in Chinese herbal medicine (CHM), integrating bitter purgative effects with warming and activating properties. They are primarily applied to warm the middle energiser, dispel cold, promote qi circulation, alleviate pain and dry dampness while strengthening the spleen, rendering them particularly effective in mixed deficiency–excess patterns, such as cold-damp accumulation with splenic dysfunction and qi–blood stasis. Their warming nature facilitates cold dispersion while their bitter constituents contribute to dampness resolution and fire clearance, producing a synergistic therapeutic profile.

Several bitter-warm herbs have also demonstrated antitumour potential. *Atractylodes lancea* exerts anticancer effects largely through atractylenolide, which suppresses tumour cell proliferation by modulating the MEK/ERK and NF-κB signalling pathways and downregulating proliferation-related protein expression.[12] *Armeniacae Semen Amarum* contains the cyanogenic glycoside amygdalin, which exerts inhibitory effects on multiple tumour cell lines, including A549, MCF7, AGS and HDF cells, by suppressing cell growth and proliferation. Mechanistically, amygdalin induces apoptosis by downregulating the mRNA expression of antiapoptotic genes, including *Survivin* and X-linked inhibitor of apoptosis protein (*XIAP*), and modulating the expression of the lncRNAs GAS5 and MALAT1.[13]

Bitter-Hot Medicinals

Bitter-hot medicinals form a distinct category defined by bitter flavour and hot thermal properties, primarily used to treat cold syndromes, such as cold-damp arthralgia and epigastric cold pain. This subclass is uncommon in clinical practice, with only three species identified in our survey: *Evodia rutaecarpa, Aconiti Kusnezoffii Radix Praeparata* and *Aconiti Radix*. These agents exert dual therapeutic effects by dispersing cold pathogens through intense thermogenic activity while their bitter components provide analgesic, qi-activating and dampness-resolving activities.

Other Medicinal Botanicals

Sweet-Property Medicinals

Sweet-property medicinals exhibit three principal therapeutic actions: tonifying deficiency states, alleviating spasmodic pain and harmonising herbal formulations. Clinically, these agents are employed to ameliorate systemic debility, relieve muscular contractures, optimise compound compatibility and modulate toxic responses. Their therapeutic efficacy derives from nourishing visceral essence to support physiological function and maintain immunological homeostasis. In acute settings, their spasmolytic properties effectively relieve tendon–muscle contracture pain while facilitating detoxification through synergistic formulation effects. In antitumour proprietary medicines, sweet herbs commonly function as tonifying components or toxicity-moderating agents. Representative botanicals include *Panax ginseng, Glycyrrhizae Radix et Rhizoma* and *Astragali Radix*.

In contemporary pharmacological studies, ginsenosides (the characteristic active constituents of ginseng) exert pronounced inhibitory effects on neoplastic proliferation and metastasis while demonstrating robust immunomodulatory activity within the tumour microenvironment.[14] *Glycyrrhiza* displays distinctive bidirectional regulatory properties, attenuating excessive heat in hot-natured formulas while tempering cold properties in cool-natured preparations. *Ligustrum lucidum* Ait. contains oleanolic acid, which exerts antitumour activity by suppressing the purine salvage pathway. Mechanistically, oleanolic acid enters cells and selectively inhibits superoxide dismutase 1 activity, thereby increasing ROS levels, activating AMPK, inhibiting mechanistic target of rapamycin complex 1 (mTORC1) and activating autophagy–lysosomal degradation pathways that degrade key enzymes involved in purine salvage, thereby suppressing DNA replication and malignant proliferation in tumour cells.[15] Conversely, *Aconiti Lateralis Radix Praeparata*, a key yang-tonifying herb, regulates triple-energiser dynamics and extraordinary meridians, exhibiting

enhanced antitumour efficacy when combined with cisplatin. Yang et al[16] reported that aconite extract induces CCL2 overexpression, which is associated with natural killer (NK) cell activation, enhancing antitumour immunity through increased NK cell infiltration into tumours.

Pungent Medicinals

Pungent medicinals, classified as yang in nature with ascending and dispersing tendencies, exhibit aromatic permeability and strong penetrative action. These features enable them to disperse exogenous cold pathogens, activate qi dynamics and resolve blood stasis. In oncological treatment, pungent herbs display "dispersing and mobilising" effects that alleviate symptoms by eliminating pathogenic factors, supporting vital qi and regulating yin–yang balance. Representative agents include *Zingiber officinale* Roscoe, *Aconiti Lateralis Radix Praeparata* and *Curcumae Longae Rhizoma*; the latter exerts blood-breaking, qi-activating and meridian-unblocking analgesia effects. Phytochemical analysis identified 85 pungent botanicals (33.9% of all specimens; Figure 1), subclassified as pungent-cold (15 species, 17.7%), pungent-cool (5 species, 5.88%), pungent-warm (45 species, 56.5%) and pungent-hot (8 species, 9.4%) variants.

Modern pharmacological research has shown that curcumin, a polyphenolic compound isolated from *Curcuma longa* L., suppresses neoplastic proliferation by inducing apoptosis through modulation of key signalling pathways, such as mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK) and phosphoinositide 3-kinase/protein kinase B (PI3K/AKT), demonstrating therapeutic activity against gastric, oral, colorectal and prostate carcinomas. Du et al[17] reported that aconitine inhibits PI3K/AKT and MAPK/ERK1/2 signalling, thereby regulating protein and mRNA expression of PCNA and apoptosis-related mediators while inhibiting tumour growth in vivo. *Houttuynia cordata* Thunb., a pungent-cold botanical, exhibits broad-spectrum antiproliferative activity via volatile oils, ethanol extracts and alkaloid fractions. Subhawa et al[18] found that Heartleaf Houttuynia Herb extract suppresses colony formation in the breast cancer cell lines MCF-7 and MDA-MB-231 and induces G1-phase cell-cycle arrest at low concentrations by downregulating cyclin D1 and CDK4 expression while also inhibiting migration and invasion through reduced MMP-2 and MMP-9 secretion. At higher concentrations, it induces apoptosis, activates caspases and upregulates related proteins.[18] Cinobufotalin from pungent-warm *Bufonis Venenum* (*Bufo gargarizans* Cantor) exhibits efficacy across multiple cancer types, with cinobufagin injections clinically applied to reduce adverse drug reactions and enhance chemotherapeutic outcomes. Toad venom components also show potent inhibition of melanoma growth by blocking metastasis. Conversely, cinnamaldehyde, the bioactive constituent of pungent-hot *Cinnamomi Cortex*, exerts diverse pharmacological effects, including antitumour, antimicrobial and antioxidant activities. Moreover, it inhibits gastric xenograft growth by inducing apoptosis via BCL-2 downregulation and caspase-dependent pathway activation.[19]

Sour-Property Medicinals

Sour-property medicinals display multiple therapeutic functions, including yin nourishment, heat clearance, astringency, fluid generation and intestinal consolidation. These agents derive from botanical, mineral and zoological sources, with plant-derived variants predominating. Two classification models exist for sour herbs: (i) intrinsically sour-tasting materia medica, represented by *Mume Fructus* and *Ziziphi Spinosae Semen*, and (ii) functionally acidic herbs characterised by astringent properties, such as *Schisandrae Chinensis Fructus, Corni Fructus* and *Granati Pericarpium*. Canonical TCM theory states that "sour flavour enters the liver", indicating regulatory effects on hepatic dispersion and blood storage, which underpin their relevance in hepatopathies. Their principal astringent and consolidating properties translate into clinical applications such as perspiration control and diarrhoea management.

Telang et al[20] reported that *Cornus officinalis* induces dose-dependent cell growth arrest and inhibits anchorage-independent colony formation. Their findings showed that *C. officinalis* extract suppresses G1 to S-phase transition in triple-negative breast cancer cells, reduces cyclin D1 and phosphorylated retinoblastoma protein expression and modulates the expression of apoptosis-related proteins BCL-2–associated X protein (Bax)/Bcl-2 while upregulating proapoptotic caspase-3/7 activity, ultimately inhibiting tumour growth.[20] Ursolic acid, a characteristic component of Chinese plum, is known to target a broad spectrum of proinflammatory transcription factors, cyclins, growth factors, kinases, cytokines, chemokines, adhesion molecules and inflammatory enzymes. These molecular targets collectively contribute to inhibiting cancer initiation, progression and metastasis.[21]

Salty-Property Medicinals

Quantitative analysis identified 21 salty-property medicinals (8.4% of all botanicals); their thermal property distribution is presented in Figure 1. Mechanistically, salty-property medicinals operate across two therapeutic dimensions: (i) intrinsically saline agents, exemplified by *Mirabilitum*, which regulate hydroelectrolyte balance, nourish yin, moisten dryness and promote diuresis in hydro-dampness disorders; and (ii) functionally inferred variants exhibiting hardness-softening and mass-dissipating properties, including the clinically important agents *Gekko japonicus, Bungarus Parvus* and *Trionycis Carapax*. Experimental studies demonstrate that lyophilised *Gekko gecko* powder markedly inhibits murine sarcoma S180, with tumour inhibition rates of 49.8%, 52.8% and 43.1% in high-, mid- and low-dose cohorts, respectively. This antitumour activity involves apoptosis induction alongside downregulation of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor expression, effectively suppressing tumour angiogenesis.[22]

Bitter Taste Receptor Mechanisms Underlying Herbal Pharmacodynamics

Taste Receptors

The "five tastes" (pungent, sweet, sour, bitter and salty) of TCM constitute a central element of its pharmacological theory. They not only reflect the sensory qualities of medicinal substances but are also associated with therapeutic actions and meridian tropism.

The "five tastes" extend beyond simple taste perception. When a medicine enters the mouth, its chemical components stimulate taste receptors in the oral cavity, activating specific taste pathways (sweet, umami, bitter, sour and salty) and generating initial gustatory signals. This process closely aligns with modern taste receptor science. Sugars in sweet-tasting herbs (eg glycyrrhizin in liquorice) activate T1R2/T1R3 sweet taste receptors. Organic acids in sour-tasting herbs (eg citric and malic acids in ume) stimulate sour taste receptors, such as the PKD2L1 channel. Alkaloids (eg berberine in *Coptis*) and glycosides in bitter-tasting herbs activate multiple bitter type 2 taste receptors (T2Rs). Inorganic salts (eg sodium sulphate in Epsom salt) in salty-tasting herbs stimulate salt-sensitive receptors, such as the ENaC channel. In contrast, pungent herbs show minimal correspondence with the classical basic tastes. Their "pungent" sensation is largely independent of traditional taste receptors and instead relies on chemesthetic perception mediated by trigeminal nerve activation. Consequently, pungent taste perception and the early onset of pharmacological responses (eg sweating) depend primarily on thermo-, cold- and pain-related sensations and neural reflexes mediated by transient receptor potential (TRP) channels rather than canonical taste receptors.

The association between taste-related chemosensory receptors underlying the five tastes in TCM (eg bitter T2Rs, sweet/umami taste T1Rs, pungent taste TRP channels, sour taste receptors and salty taste ENaC) and cancer is an emerging research domain. These receptors are not confined to the oral cavity; they are widely expressed throughout bodily tissues, including tumour cells and the tumour microenvironment, where they participate in regulating tumour initiation, progression, metastasis and therapeutic responsiveness. Sweet taste receptors are also implicated in tumour regulation. For example, L-amino acids enhance NK cell–mediated cytotoxicity against tumour cells via T1R1/T1R3 receptors, and T1R3 inhibits the activity of human gastric adenocarcinoma cells.[23,24] Salt taste receptors similarly show relevance to antitumour therapy. Ware et al[25] reported that elevated ENaC expression suppresses breast cancer cell proliferation. Acid-sensitive and pungent receptors are likewise involved in antitumour mechanisms, with both classes converging on TRPV1 signalling. In nude mouse models, TRPV1 exhibited antigastric cancer activity, with molecular mechanisms potentially underlying this effect.[26,27]

Bitter Taste Receptors

Gustatory bitterness perception is mediated by T2Rs expressed on taste bud cells. Upon ligand engagement, T2Rs initiate intracellular signalling cascades that culminate in central nervous system recognition of bitter stimuli. Structurally, T2Rs possess a characteristic seven-transmembrane helical architecture, in which a single polypeptide chain forms transmembrane domains connected by three extracellular and three intracellular loops that stabilise receptor conformation.[28] Notably, taste receptor type 2 (TAS2R) 14 possesses two distinctive ligand-binding pockets: (i) an orthosteric site on the plasma membrane occupied by cholesterol molecules and (ii) an intracellular allosteric site accommodating smaller

ligands. Mechanistically, cholesterol binding preactivates TAS2R14 into a semi-active state, sensitising the receptor to subsequent bitter agonist binding and facilitating neural signal transmission.

Phytochemical constituents of bitter herbs directly regulate T2R-mediated signalling, with experimental evidence confirming interactions between T2Rs and numerous bitter phytocompounds. Representative examples include bitter principles from *Artemisia absinthium*, notably picrotoxinin among eight identified compounds, binding human bitter T2R (hT2R) 14;[29,30] aristolochic acid activating hT2R43/hT2R44;[31] and aloin functioning as an agonist of hT2R43.[32] These findings establish T2R-dependent activation as a fundamental mechanism underlying bitter taste perception of herbal medicines. *Strychnos nux-vomica*, containing the prototypical T2R agonist strychnine, exhibits exceptionally high affinity for TAS2R46. Importantly, TAS2R46 possesses a unique activation switch that enables broad-spectrum ligand recognition, representing an evolutionary adaptation for rapid toxic compound detection.[30]

T2Rs, classified in the G protein–coupled receptor superfamily, were initially characterised in taste bud cells as mediators of bitter gustation.[33] Subsequent studies have revealed their evolutionarily conserved roles in detecting toxic substances, monitoring metabolic disturbances and initiating defence responses against infectious agents.[34] Beyond chemosensory perception, T2Rs have diverse extragustatory functions. In immunomodulation, they serve as activation targets whereby bitter agonists induce calcium influx–dependent nitric oxide release and guanylate cyclase activation, accelerating phagocytosis and enhancing antimicrobial defence. Conversely, T2Rs also exhibit immunosuppressive effects, as increased expression in asthmatic airways correlates with reduced proinflammatory cytokine secretion, with studies on alveolar macrophages derived from patients with cancer confirming T2R-mediated inhibition of cytokine production.[35] In the gastrointestinal system, T2Rs detect luminal stimuli to regulate motility and secretion, thereby supporting nutrient absorption and metabolic waste clearance. In reproductive physiology, progesterone acts as an agonist at TAS2R110/114 receptors,[36] regulating gestational timing through immunomodulation and placental hormone secretion that influence foetal development. Functional T2Rs with canonical signalling components, ie α-gustducin, phospholipase C beta 2, transient receptor potential cation channel subfamily M member 5 (TRPM5) and inositol 1,4,5-trisphosphate receptor type 3, are expressed in murine and human myometrium, where the bitter agonist chloroquine induces concentration-dependent uterine relaxation exceeding that of conventional tocolytics.[37] In the central nervous system, T2Rs are distributed across the brainstem, hypothalamus, cerebral cortex, cerebellum, nucleus accumbens, hippocampus and choroid plexus epithelial cells,[38] highlighting their potential roles in neurogenesis and neural repair. Although T2Rs primarily mediate bitter taste perception, their extraoral expression orchestrates complex physiological regulation across immune, gastrointestinal, reproductive (Figure 2) and neural systems via transcriptional and posttranslational mechanisms essential for systemic homeostasis.[39]

Cancer-Specific Modulation of Bitter Taste Receptor Signalling

Associations between bitter taste receptors and tumour types were analysed using Origin software (Figure 3). Colorectal cancer exhibited significant associations with seven bitter taste receptors (TAS2R4, TAS2R5, TAS2R14, TAS2R19, TAS2R20, TAS2R31 and TAS2R38). Similarly, head and neck squamous cell carcinoma was linked to seven distinct receptors (TAS2R4, TAS2R14, TAS2R19, TAS2R20, TAS2R30, TAS2R43 and TAS2R45). In contrast, breast carcinoma showed associations with six receptors (TAS2R1, TAS2R4, TAS2R10, TAS2R14, TAS2R38 and TAS2R49/20). Notably, most other cancer types, except pancreatic and thyroid carcinomas, displayed multiple bitter taste receptor associations. Collectively, these findings indicate a potentially important role for bitter taste receptors in cancer pathogenesis.

Breast Carcinoma

T2R expression profiles differ markedly between malignant and normal mammary epithelial cells, with quantitative real-time polymerase chain reaction and flow cytometry analyses revealing significant downregulation of T2R1, T2R4, T2R10, T2R38 and T2R49 in neoplastic tissues.[40] Pharmacological activation of these receptors by cognate bitter agonists induces intracellular calcium mobilisation, and multiple bitter phytocompounds exert antitumour effects through inhibition of proliferation and induction of apoptosis. Although the precise regulatory role of T2Rs in the breast cancer microenvironment remains incompletely defined, their systemic downregulation may synergistically promote tumour progression, positioning T2Rs as potential targets for anticancer therapy.

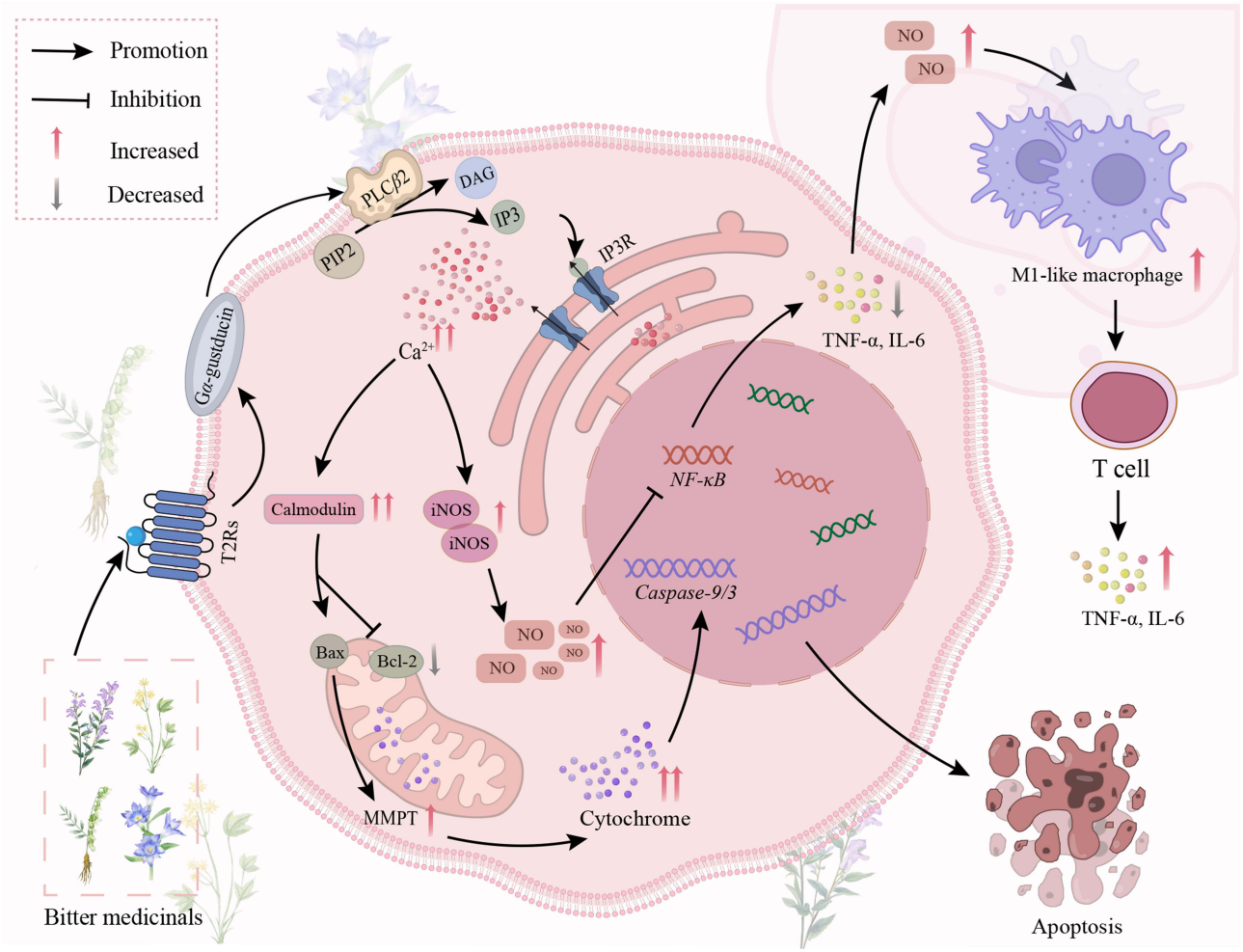

Figure 2 Mechanisms underlying bitter taste receptor activity. Anti-inflammatory and immunomodulatory effects mediated by bitter taste receptor (TAS2R) activation are triggered by bitter medicinal compounds. Bitter constituents activate bitter TAS2Rs, initiating a signalling cascade involving Gα-gustducin, PLCβ2 and IP3-mediated Ca^{2+} release. The resulting increase in intracellular Ca^{2+} activates calmodulin-dependent pathways, enhancing nitric oxide (NO) production and modulating NF-κB/iNOS signalling. These responses collectively suppress proinflammatory cytokine expression and inhibit M1-like macrophage polarisation. Concurrently, elevated Ca^{2+} and NO levels promote apoptosis of overactivated immune cells via mitochondrial pathway regulation.

Neuroblastoma

Neuroblastoma, an aggressive paediatric extracranial solid tumour with poor prognosis, exhibits reduced cancer stemness following TAS2R8 or TAS2R10 overexpression.[41] Experimental studies have demonstrated that enforced TAS2R8 expression decreases transcript levels of delta-like noncanonical notch ligand 1, CD133, neurogenic locus notch homolog protein 1 and sex determining region Y-box 2, correlating with attenuated tumorigenicity in vivo. Notably, nude mouse xenograft formation rates declined from 100% to 20% with TAS2R8 overexpression and to 70% following TAS2R10 induction. This tumour-suppressive effect involves inhibition of invasion pathways and modulation of hypoxic micro-environments, highlighting the therapeutic potential of targeting T2Rs in neuroblastoma management.

Head and Neck Squamous Cell Carcinoma

Head and neck squamous cell carcinoma (HNSCC) is increasing in incidence, particularly among females. T2R genes, including *TAS2R4, TAS2R14* and *TAS2R20*, display heterogeneous expression patterns across patient samples and cell lines, with certain receptors exhibiting tumour-specific upregulation.[42] Bitter agonist stimulation induces dysregulated calcium transients in HNSCC cells, resulting in nuclear calcium overload that leads to mitochondrial dysfunction and caspase-dependent apoptosis. This calcium-mediated cytotoxic mechanism underscores the therapeutic relevance of T2R modulation in epithelial malignancies.

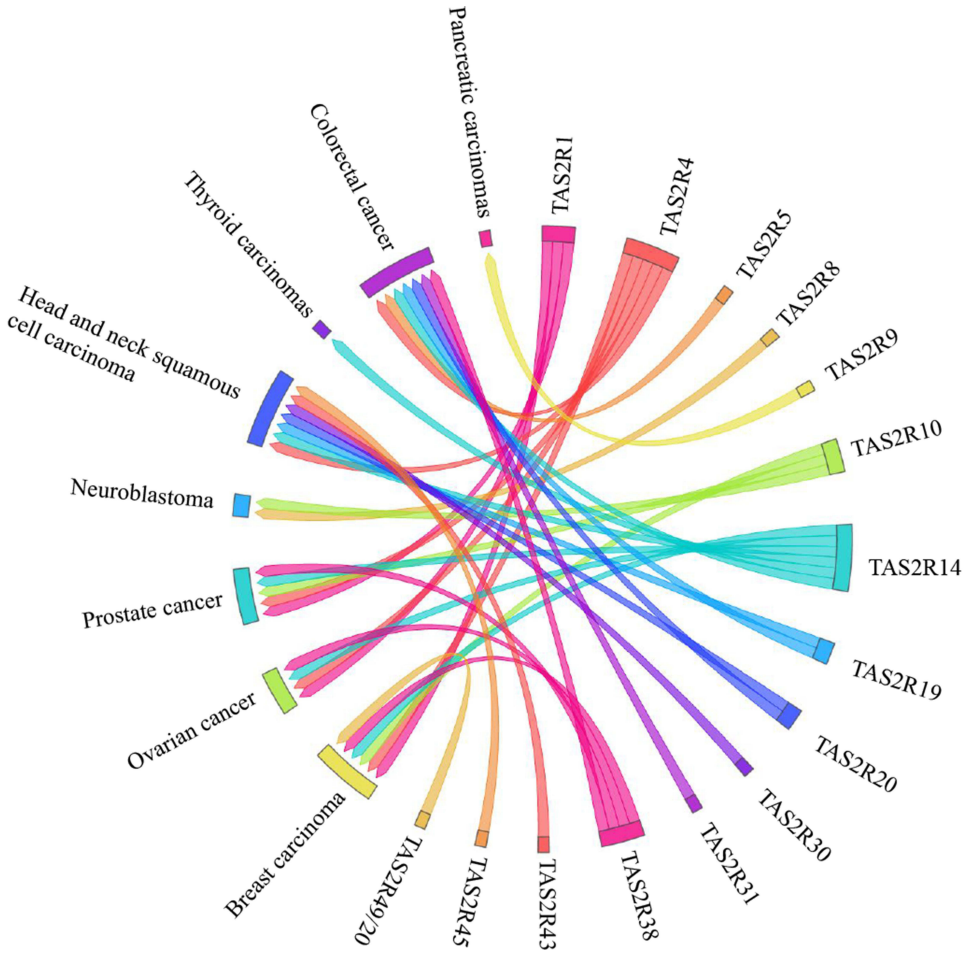

Figure 3 Reported associations between functionally characterised bitter taste receptors and distinct cancer types. Expression of 16 bitter taste receptors (TAS2Rs), including TAS2R1, TAS2R4 and TAS2R5, across common human tumours (eg breast cancer). Arrows indicate associations between individual TAS2Rs and corresponding tumour types.

Colorectal Cancer

In colorectal cancer (CRC), the second leading cause of cancer-related mortality worldwide, overexpression of seven TAS2Rs genes (*TAS2R4, TAS2R5, TAS2R14, TAS2R19, TAS2R20, TAS2R31* and *TAS2R38*) has been reported in malignant tissues.[43] Transcriptional profiling stratifies patients with CRC into two molecular subtypes: subtype A shows elevated TAS2R expression associated with poorer survival, whereas subtype B exhibits lower expression linked to more favourable outcomes. This inverse association between TAS2R abundance and patient survival highlights their value as prognostic biomarkers and potential therapeutic targets in CRC.

Ovarian Cancer

Ovarian cancer, the most lethal gynaecologic malignancy, shows marked downregulation of *TAS2R1, TAS2R4, TAS2R14* and *TAS2R38* mRNA compared with normal ovarian epithelium.[44] Pharmacological activation of TAS2R14 by noscapine initiates G protein–coupled receptor–mediated calcium release, subsequently upregulating proapoptotic proteins, including Bax and BCL-2 homologous antagonist/killer while suppressing antiapoptotic factors, such as BCL-2 and myeloid cell leukaemia 1, ultimately inducing dose-dependent reductions in ovarian cancer cell viability.

Prostate Cancer

Prostate cancer, the sixth most prevalent malignancy in males, shows downregulation of most TAS2Rs, except preserved TAS2R38 expression in PC3 cells.[44] Noscapine-induced TAS2R14 agonism similarly triggers calcium-dependent

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apoptosis in prostate adenocarcinoma cells, with functional studies confirming that TAS2R14 overexpression enhances noscapine cytotoxicity, whereas receptor knockdown diminishes its therapeutic efficacy. Collectively, these findings position TAS2R14 as a tractable target for noscapine-based interventions in ovarian and prostate carcinomas, warranting further investigation of long-term effects and in vivo mechanisms.

Thyroid Carcinomas

Globally, thyroid carcinoma incidence is steadily increasing, posing major challenges to public health systems. Liu et al[45] reported significantly reduced TAS2R14 mRNA and protein expression levels in malignant thyroid tissues relative to normal tissues, with immunohistochemical analyses confirming receptor downregulation across papillary and follicular subtypes. Critically, patients with low TAS2R14 expression exhibited superior overall survival relative to high-expression cohorts (hazard ratio: 0.62; 95% confidence interval: 0.48–0.79; $P < 0.001$), establishing TAS2R14 as an independent prognostic biomarker in multivariable regression models adjusting for age, tumour stage and histological subtype. These findings position TAS2R14 expression as a potential predictor for clinical outcome in thyroid cancer, meriting prospective validation in multi-institutional cohorts to refine risk stratification and therapeutic decision-making.

Pancreatic Carcinoma

Pancreatic ductal adenocarcinoma (PDAC), often referred to as the "king of cancers" owing to its insidious onset and frequent late-stage diagnosis with limited operability, exhibits exceptionally high mortality and few effective treatment options. Studies by Stern et al[46] and Gaida et al[47] demonstrated tumour-specific overexpression of T2R10 and T2R38 in human PDAC specimens, with these receptors absent from normal exocrine pancreas parenchyma. Notably, caffeine-mediated agonism of these ectopically expressed T2Rs enhances chemosensitivity in pancreatic carcinoma models, suggesting T2R10/T2R38 activation as a novel adjuvant strategy to potentiate conventional cytotoxic therapies.

Research Progress on Bitter-Tasting Herbal Medicines

For most TCMs, an intrinsic relationship exists between pharmacological bitterness and gustatory bitter taste, with bitter phytoconstituents forming the material basis of therapeutic efficacy. Current research on bitter-property herbs largely adopts chemical and biological perspectives, employing component fractionation approaches to elucidate associations between defined phytochemical classes and the material foundations underlying bitter properties. The solanine component present in the lantern plant represents the principal substance responsible for its antibacterial activity. Fu et al[48] reported that solanine inhibits constitutive STAT3 activity, thereby suppressing STAT3-induced downstream gene expression and producing pronounced antitumour effects against non-small cell lung cancer and multiple myeloma cells by enhancing tumour cell apoptosis.

The active component schisandrin B in *S. nux-vomica* also exhibits marked antitumour activity. Lü et al[49] showed that schisandrin B inhibits A549 cell proliferation in a dose-dependent manner by downregulating cyclin D1, CDK4 and CDK6 expression while upregulating p53 and p21, thereby inducing G0/G1 phase cell-cycle arrest. It additionally increases the expression of Bax, cleaved caspase-3 and −9 and cytochrome C while decreasing Bcl-2 and PCNA expression, ultimately triggering apoptosis. Furthermore, schisandrin B suppresses invasion and migration of A549 cells through downregulation of HIF-1, VEGF, MMP-9 and MMP-2 expression.[49]

Notably, bitter principles frequently overlap with bioactive components in numerous bitter herbs. Berberine, the primary bitter agent in *Coptis chinensis* Franch., simultaneously mediates antimicrobial and dampness-drying antidiarrheal effects; andrographolide, the principal bitter compound in *Andrographis paniculata*, functions as the key active substance responsible for heat-clearing, detoxifying, anti-inflammatory and analgesic actions. Molecular studies have shown widespread extraoral distribution of bitter TAS2Rs within gastrointestinal epithelia, where bitter agonists activate receptor-mediated signalling cascades to initiate physiological responses. In enteroendocrine STC-1 cells expressing multiple TAS2R genes, bitter stimulation promotes activation of voltage-gated L-type calcium channels, inducing rapid intracellular calcium mobilisation. This calcium influx facilitates TRPM5 channel opening, leading to membrane depolarisation and subsequent neurotransmitter release that conveys chemosensory signals to the central nervous system.[50]

Flavonoids

Flavonoids constitute a critically important class of natural organic compounds with broad pharmacological properties and substantial therapeutic potential across diverse human diseases. This section focuses on their application in antineoplastic interventions. The chemopreventive and anticancer activities of flavonoids are primarily mediated through three mechanisms: free radical scavenging, direct suppression of neoplastic cell proliferation and antagonism of carcinogenic factors.[51] Functioning as potent antioxidants and free radical scavengers, flavonoids effectively attenuate lipid peroxidation–induced cellular damage, thereby conferring protection against carcinogenesis.

Flavonoid constituents derived from *Sophora flavescens* exhibit marked antitumour activity. When coadministered with paclitaxel, these compounds synergistically enhance the chemotherapeutic agent's inhibitory effects on tumour growth.[52] Zhang et al[53] isolated a novel flavonoid, (2S)-7,2',4'-trihydroxy-5-methoxy-8-dimethylallylflavanone (compound 1), from *S. flavescens*, which displayed substantial anticancer activity. Compound 1 inhibits cell proliferation, migration, adhesion and tube formation, induces G0/G1 phase cell-cycle arrest and downregulates VEGF expression, thereby exerting anticancer effects.[53]

Astragalus flavonoids similarly regulate the human immune system and suppress tumour progression. These flavonoids inhibit breast cancer cell growth and proliferation in a dose-dependent manner and prolong survival in nude mouse models.[54] Additional flavonoid constituents in *Astragalus*, including formononetin, calycosin, calycosin-7-O-β-D-glucopyranoside, formononetin-7-O-β-D-glucopyranoside and huangliangjiangsu, display varying degrees of antitumour activity. Park et al[55] examined the toxicological effects and mechanisms of formononetin in ovarian cancer ES2 and OV90 cells, showing that formononetin induces G0/G1 phase arrest and promotes apoptosis. Moreover, it inhibits tumour development and metastasis through regulation of tumour marker genes, including *ERK1/2, P90RSK* and *p-p38*. Mao Rui isoflavones also exhibit pronounced antitumour effects, as treatment with Mao Rui isoflavone derivatives suppresses the proliferation, migration and invasion of melanoma cells while inducing apoptosis.[56]

Alkaloids

Alkaloids comprise a class of naturally occurring, nitrogen-containing organic compounds with alkaline properties. This section focus on their roles in antitumour therapy. Alkaloids, such as vinblastine, vincristine and vinorelbine, extracted or semi-synthesised from the *Vinca* species, have been successfully applied clinically for the treatment of leukaemia and solid tumours. Vincristine demonstrates high efficacy against acute lymphoblastic leukaemia, with its mechanism involving disruption of microtubule stability and arrest of the cell cycle at the G2/M phase.[57]

Zhang et al[58] reported that matrine induces dose-dependent downregulation of the antiapoptotic protein Bcl-2 while upregulating the proapoptotic protein Bax, thereby reducing the Bcl-2/Bax protein ratio in A549 and SMMC-7721 cells. Matrine also inhibits A549 cell migration without compromising cell viability. Owing to its relatively low toxicity, matrine has been widely used clinically and can be combined with chemotherapy to reverse multidrug resistance in tumour cells.

The alkaloid SG in *S. nux-vomica* induces apoptosis and necrosis in tumour cells.[59] Both *S. flavescens* and *Sophora japonica* contain oxymatrine. Guo et al[60] demonstrated that oxidised matrine targets the Tyr845 phosphorylation site of EGFR in gastric cancer cells, inhibiting EGFR activation and downstream Ras/Raf/ERK and PI3K/Akt/mTOR signalling pathways. This inhibits the proliferation, migration and invasion of gastric cancer cells in a dose-dependent manner and induces apoptosis in lung cancer cells.[60] Oxycoryneine exerts antiangiogenic effects by inhibiting the Nrf2/HO-1 signalling pathway in oral squamous cell carcinoma cells.[61] Lily alkaloids similarly inhibit human gastric cancer SGC-7901 cells in a time- and dose-dependent manner by inducing G2/M phase arrest, upregulating caspase-3 protein expression and downregulating Fasl protein levels, thereby promoting apoptosis and suppressing cancer cell proliferation.[62]

Glycosides

Glycosides are a class of natural products characterised by broad-spectrum bioactivities. Structurally, they consist of a glycone moiety (eg glucose) linked via a glycosidic bond to an aglycone component. Based on aglycone diversity, glycosides are categorised into cardiac glycosides, saponins and flavonoid glycosides. Certain glycosides exert

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antitumour effects by suppressing tumour-associated angiogenesis. For instance, polyphyllin II markedly reduces VEGF levels in ovarian carcinoma and embryonic cells, demonstrating time- and dose-dependent inhibition of VEGF-induced proliferation, migration and tube formation in human umbilical vein endothelial cells.[63]

Kim et al[64] identified steroidal saponins from aqueous extracts of *Asparagus cochinchinensis*, with asparacochioside A exhibiting pronounced cytotoxicity against human ovarian cancer A2780 cells. Similarly, Zhang et al[65] isolated protodioscin from 90% ethanolic extracts of *A. cochinchinensis*, demonstrating cytotoxicity and antiproliferative effects in human hepatocellular carcinoma MHCC97H and lung adenocarcinoma H1299 cell lines. Additional steroidal saponins derived from *A. cochinchinensis*, including nicotianoside B, immunoside and C-27 spirostanol saponins, further inhibit proliferation of human cervical cancer HeLa cells.

Mangiferin, a flavonoid glycoside derived from *Anemarrhena asphodeloides*, suppresses proliferation across multiple malignancies, including lung, prostate, cervical and ovarian carcinomas. Its anticancer mechanisms involve downregulation of oncogenic miRNAs (miR-92a and miR-27b) alongside upregulation of the tumour suppressor gene *period1*, thereby regulating cancer cell proliferation and apoptosis. Concurrently, mangiferin induces G2/M phase cell-cycle arrest through downregulation of cyclin B1.[66,67]

Terpenoids

Terpenoids constitute a widespread class of bitter principles in TCM, structurally defined by isoprene units and classified into monoterpenes, sesquiterpenes, diterpenes, triterpenes and tetraterpenes. Accumulating evidence substantiates their pronounced antitumour efficacy.[68] Paclitaxel, a tetracyclic diterpenoid, operates via a mechanism distinct from conventional chemotherapeutic agents, as it neither interferes with DNA/RNA synthesis nor directly damages DNA molecules. Instead, paclitaxel primarily promotes tubulin polymerisation. By selectively binding β-tubulin, it enhances microtubule assembly and stabilisation, thereby depleting soluble tubulin pools. This process disrupts spindle formation, induces G2/M phase mitotic arrest and ultimately triggers neoplastic cell death.

Oridonin, another bioactive diterpenoid, effectively suppresses tumour growth in murine models. Mechanistically, oridonin increases the Bax/BCL-2 ratio to initiate apoptosis while simultaneously inhibiting mTORC1 activity, thereby eliciting antitumour responses.[69] Triptolide, a well-studied diterpene derived from *Tripterygium wilfordii*, suppresses overexpression of mouse double minute 2 homolog in gastric carcinoma cells. This suppression stabilises p53 protein levels and downregulates XIAP, thereby inducing p53-dependent apoptosis.[70] Furthermore, triptolide promotes cytochrome c release and caspase-3 activation in ovarian cancer A2780 cells, concomitant with S-phase cell-cycle arrest.[71] Collectively, the potential pharmacological mechanisms of bitter-tasting TCMs are summarised in Figure 4.

Meridian Tropism Analysis of Antitumour Herbal Medicines

Meridian tropism analysis across 11 categories revealed predominant affinity for the heart, liver, spleen, lung and kidney meridians. Herbal medicines targeting the liver meridian predominated (146 substances, 58.2%), followed by the lung meridian (94 substances, 37.5%), spleen meridian (86 substances, 34.3%), kidney meridian (77 substances, 30.7%) and heart meridian (73 substances, 29.1%). Meridian tropism theory elucidates the tissue and organ selectivity of pharmacologically active compounds by describing their directional affinity towards specific zang-fu organs and meridian systems.

Statistical analysis by Lei et al[72] on 205 commonly used herbs demonstrated significant correlations between meridian tropism and anatomical target specificity. Agents acting on the cardiovascular, haematological and haematopoietic systems predominantly exhibited liver meridian tropism; herbs modulating digestive function aligned with the stomach meridian; and respiratory therapeutics preferentially targeted the lung meridian. Liver meridian–related clinical studies have indicated that transcutaneous electrical acupoint stimulation applied to liver meridian acupoints in patients with hepatocellular carcinoma alleviates cancer-related pain while improving functional status and quality of life. These therapeutic effects are primarily linked to modulation of hepatic microcirculation and suppression of inflammatory responses. Mechanistically, electroacupuncture activates the liver meridian–spinal cord–brainstem pain inhibitory pathway, downregulates proinflammatory mediators (such as TNF-α and COX-2) and inhibits hepatic stellate cell activation, thereby contributing to symptom control and optimisation of the tumour microenvironment.[72]

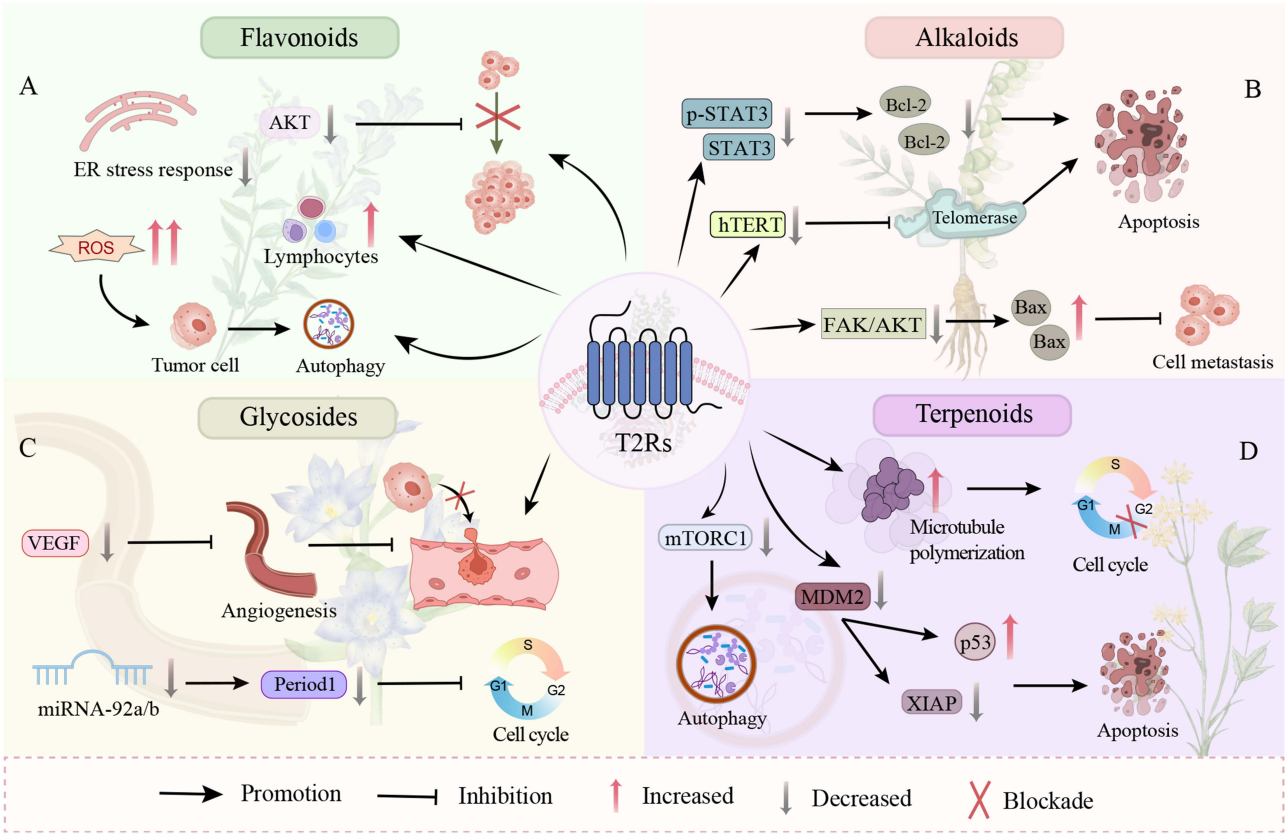

Figure 4 Mechanisms of action of bitter-tasting herbal medicines. Bitter phytochemicals, including flavonoids, alkaloids, glycosides and terpenoids, may activate TAS2Rs expressed in tumour cells and within the tumour microenvironment. (**A**) Apoptosis and autophagy induction. (**B**) Suppression of angiogenesis and metastasis. (**C**) Cell-cycle arrest. (**D**) Immunomodulation within the tumour microenvironment.

The lung meridian similarly contributes to alleviation of cancer-related complications. In patients with upper-limb lymphoedema following breast cancer surgery, moxibustion at the Lieque (LU7) acupoint increases serum VEGF-C levels and enhances lymphatic circulation, consistent with the traditional concept that the lungs regulate fluid distribution. In lung cancer, lung meridian–based interventions mitigate respiratory symptoms by modulating airway smooth muscle receptor activity and reducing inflammatory mediator release. These effects align closely with interfascial fluid transport pathways corresponding to the lung meridian, supporting functional associations between meridian trajectories, organ regulation and molecular targets.[73]

Additionally, contemporary research supports the involvement of other meridians in cancer protection and systemic regulation. Heart meridian–associated herbs, such as ginseng, mitigate chemotherapy-induced cardiotoxicity by regulating myocardial Na^+/K^+-ATPase activity and suppressing apoptosis-related signaling.[14,74] Spleen meridian–related herbs, including astragalus[54] and atractylodes,[12] enhance gastrointestinal function and immune competence through activation of the AMPK pathway, restoration of gut microbiota homeostasis and augmentation of T-lymphocyte subsets. Kidney meridian–associated *Ligustrum lucidum* fruit[11] confers renoprotective effects by inhibiting renal tubular epithelial apoptosis, regulating aquaporin expression and strengthening antioxidant capacity, thereby supporting systemic resilience during cancer therapy. Collectively, this evidence supports the notion that meridian classification predicts pharmacological organotropism. As historically articulated by Xu Lingtai: "Ignorance of meridians in medication leads to non-specific efficacy; rigid adherence to meridian dogma may induce therapeutic harm".

Conclusions and Future Perspectives

Compared with prior research, the targets predicted through database analysis in this study showed certain discrepancies. Candidate targets were obtained from curated databases, and corresponding visualisations were generated. Specifically,

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The Human Gene Database (GeneCards) was used to identify receptors associated with major malignancies, such as lung, breast and liver cancer, which pose substantial health risks. These receptors were then collected and systematised. Prior studies indicate that humans possess approximately 25 bitter taste receptors,[75,76] which were compiled for comparative analysis. The Venny 2.1.0 online platform was subsequently employed to determine the intersection between cancer-related targets and known bitter taste receptors. Intersecting receptors were extracted, organised and visualised using Origin software, with binary values denoting the presence or absence of overlap. During data processing, receptors lacking intersection were excluded, yielding a final panel of candidate receptors: TAS2R1, TAS2R2, TAS2R3, TAS2R4, TAS2R5, TAS2R8, TAS2R10, TAS2R13, TAS2R14, TAS2R16, TAS2R19, TAS2R20 and TAS2R38.

As illustrated in Figure 5, lung cancer (linked to TAS2R1, TAS2R3, TAS2R4, TAS2R5, TAS2R10, TAS2R13, TAS2R14, TAS2R16, TAS2R19, TAS2R20 and TAS2R38), kidney cancer (associated with TAS2R1, TAS2R2, TAS2R3, TAS2R4, TAS2R5, TAS2R8, TAS2R10, TAS2R13, TAS2R14, TAS2R16 and TAS2R20) and gastric cancer (linked to TAS2R1, TAS2R3, TAS2R4, TAS2R5, TAS2R10, TAS2R14, TAS2R16, TAS2R19 and TAS2R38) displayed the strongest associations with bitter taste receptors, ranking first, second and third, respectively. Other cancer types, although less strongly associated compared with the first three, also showed varying degrees of linkage with bitter taste receptors. Among these, TAS2R4, TAS2R38 and TAS2R14 appeared most frequently across cancer types (Figure 3: statistical chart of bitter taste receptors associated with tumour suppression based on existing evidence).

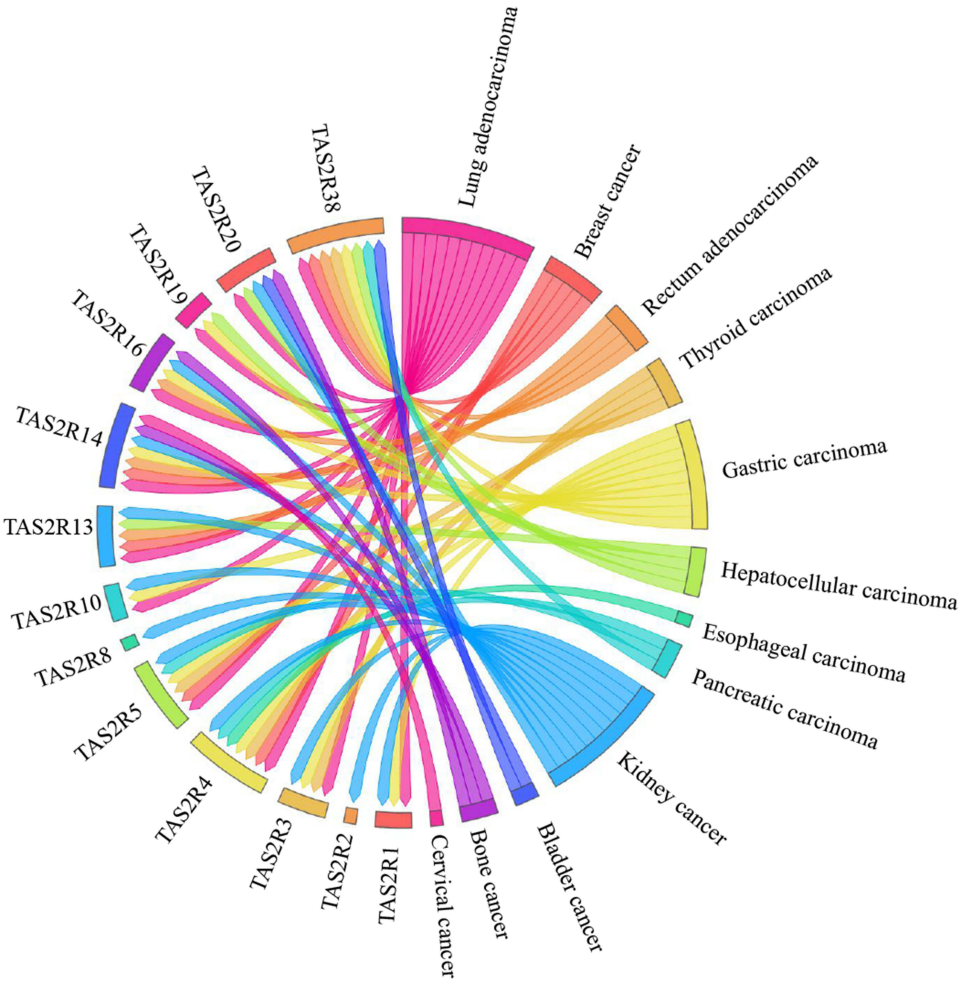

Figure 5 Predicted associations between bitter taste receptors and common cancer types based on database mining. Candidate targets were identified through database mining using the TCMSP and GeneCards databases. Bitter taste receptors potentially associated with 12 common cancer types were retrieved from GeneCards, and these cancer-related targets were intersected with known bitter taste receptors using the Venny tool to identify overlapping genes. Arrows indicate associations between cancer types and corresponding bitter taste receptors.

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Bitter-tasting herbs constitute a critical component of TCM. Current evidence indicates that specific noncovalent interactions, including hydrogen bonding, hydrophobic interactions, π–π stacking, coordination bonds and electrostatic forces, drive molecular self-assembly into structurally ordered aggregates (SAs) within these herbs. Such supramolecular architectures are widely present in biological systems, including cellular membranes and DNA double helices, and frequently display enhanced bioactivity following assembly. For instance, self-assembled aggregates of berberine and cinnamic acid exhibit superior antibacterial efficacy against *Staphylococcus aureus* compared with their monomeric forms. Similarly, coassembled nanostructures of ursolic acid (a pentacyclic triterpenoid) and paclitaxel markedly improve drug-loading capacity while preserving the antitumour and hepatoprotective functions of the acid. Notably, SA formations identified in classical decoctions (eg Huanglian Jiedu Tang, Maxing Shigan Tang and Baihu Tang) correlate with enhanced therapeutic outcomes, attributable to optimised pharmacokinetic behaviour and target engagement.

Flavonoid- and terpenoid-derived SAs from bitter herbs, including *Prunella vulgaris, Hedyotis diffusa* and *Scutellaria baicalensis*, exhibit marked antitumour efficacy against lung, breast, hepatic and colorectal carcinomas across diverse preclinical models.[77] Mechanistically, SAs enhance cytotoxicity towards malignant cells by improving cellular uptake efficiency and prolonging systemic exposure. Crucially, SA-based strategies address the limited solubility and poor bioavailability that constrain many antitumour phytochemicals, positioning this approach as a promising avenue for oncological drug development. Bioinformatics analyses further revealed abundant expression of bitter TAS2Rs in neoplastic tissues, highlighting their potential utility as therapeutic targets. Nevertheless, research on SAs remains preliminary, and the fundamental mechanisms governing assembly dynamics and structure–activity relationships require clarification through systematic investigation. Future studies addressing these knowledge gaps could advance human health through the rational engineering of phytotherapeutic nanomaterials.

TCM exhibits strong conceptual alignment with the principles of precision medicine in contemporary oncology. Through its holistic therapeutic framework, TCM exerts regulatory effects on tumour proliferation, apoptosis and the immune microenvironment via the multitarget actions of bioactive herbal constituents. Notably, the organ-selective attributes embedded in meridian theory parallel the underlying rationale of modern targeted cancer therapies. As noted by Sonkind et al[78] oncology has evolved from predominantly cytotoxic modalities towards a diversified and personalised treatment paradigm encompassing surgery, radiotherapy, chemotherapy, targeted therapy and immunotherapy. This evolution provides technical and theoretical support for the modernisation of TCM-based interventions.

Future research should prioritise the integrative development of TCM and modern oncology.[79] Application of molecular biology and systems biology approaches may clarify the scientific basis of the TCM theory of "nature, flavour and meridian tropism", including specific interactions between bitter-tasting herbal components and TAS2R family receptors. Such efforts could identify molecular targets underlying meridian-guided regulation of tumour signalling pathways and establish biomarkers supporting the precise clinical deployment of TCM. Concurrently, incorporation of TCM's holistic regulatory principles into conventional cancer management through herbal compound formulations and acupuncture may improve immune competence and correct nutrient absorption disorders as well as alleviate radiotherapy- and chemotherapy-induced gastrointestinal toxicity and fatigue. Furthermore, advanced delivery technologies, such as SAs, may be leveraged to improve the solubility and bioavailability of active TCM compounds, thereby augmenting their therapeutic efficacy. Overall, this integrative framework underscores the potential of combining traditional medical theory with modern technology to achieve safer and more effective oncological treatments.

Within the precision medicine paradigm, coordinated advances in biomarkers and companion diagnostics (CDx) have opened new avenues for cancer therapy and offer strategic opportunities for TCM modernisation.[80] Molecular features associated with bitter-tasting TCMs, particularly members of the TAS2R receptor family, represent actionable targets for CDx development, enabling patient stratification and prediction of responsiveness to TCM-based interventions. Therefore, integration of TAS2R-guided CDx screening with SA-optimised delivery constitutes a rational precision strategy for developing TCM-derived anticancer agents. This approach supports targeted clinical application of TCM and establishes a molecularly informed framework for its incorporation into precision oncology.

Molecular profiling technologies have advanced substantially in cancer early detection, prognostic evaluation and therapeutic decision-making, thereby providing a robust molecular foundation for precision oncology.[81] Building on these developments, integrating molecular profiling data with the pharmacological attributes and bioactive constituents of

TCM may facilitate a transition towards more targeted TCM-based interventions. Such integration could enable bioactive compounds to preferentially target tumour cells while minimising off-target effects on normal tissues. Moreover, development of individualised TCM intervention strategies informed by patient-specific molecular profiles may support personalised therapy, reduce immune incompatibility or therapeutic resistance and ultimately improve clinical outcomes and quality of life. Additionally, in individuals at elevated risk owing to inherited cancer susceptibility, molecular profiling–guided preventive TCM interventions may represent a promising strategy for cancer risk mitigation prior to disease onset.

In summary, CHM shows distinctive antitumour potential grounded in holistic regulation and syndrome-based differentiation. In our analysis of 251 antitumour botanical agents, 47% were classified as bitter, with bitter-cold medicines predominating, providing a rationale for precision selection and dosing in clinical contexts. Bitter taste receptors (ie TAS2Rs) are increasingly implicated in tumorigenesis and prognosis and may function as biomarkers and therapeutic targets. Consistent with this notion, key CHM constituents, such as flavonoids and alkaloids, exhibit antitumour activity via multiple mechanisms. Moreover, structurally organised SAs can enhance phytochemical solubility and bioavailability, highlighting opportunities for formulation optimisation. Future investigations should clarify SA assembly mechanisms and in vivo fate as well as defining molecular interactions between bitter constituents and TAS2Rs, thereby advancing mechanism-driven development and clinical translation of CHM-derived antitumour therapies.

Abbreviation

AKT, Protein Kinase B; AMPK, Adenosine Monophosphate-Activated Protein Kinase; BCL-2, B-Cell Lymphoma-2; Bax, BCL-2-Associated X Protein; Bak, BCL-2 Homologous Antagonist/Killer; bFGF, basic Fibroblast Growth Factor; CDK, Cyclin-Dependent Kinase; CCL2, C-C Motif Chemokine Ligand 2; CRC, Colorectal Cancer; CI, Confidence Interval; CHM, Chinese herbal medicine; ERK, Extracellular Signal-Regulated Kinase; EGFR, Epidermal Growth Factor Receptor; ENaC, Epithelial Sodium Channel; gui jing, Channel Tropism; GeneCards, The Human Gene Database; HIF-1α, Hypoxia-Inducible Factor-1α; hT2R, human bitter Taste Receptor type 2; HNSCC, Head and Neck Squamous Cell Carcinoma; HR, Hazard Ratio; ICAT, Inhibitor of β-Catenin and TCF; IP3, Inositol 1,4,5-Trisphosphate; IP3R3, Inositol 1,4,5-Trisphosphate Receptor type 3; LU7, Lieque; MEK, Mitogen-Activated Protein Kinase Kinase; MAPK, Mitogen-Activated Protein Kinase; MDM2, Mouse Double Minute 2 Homolog; miRNA, MicroRNA; mTORC1, Mechanistic Target of Rapamycin Complex 1; MCL-1, Myeloid Cell Leukemia 1; MMP, Matrix Metalloproteinase; NF-κB, Nuclear Factor-κB; NK, Natural Killer; Notch1, Neurogenic Locus Notch Homolog Protein 1; PD-1, Programmed Death 1; PD-L1, Programmed Death-Ligand 1; PI3K, Phosphoinositide 3-Kinase; PER1, Period 1; PCNA, Proliferating Cell Nuclear Antigen; PLCβ2, Phospholipase C beta 2; PDAC, Pancreatic Ductal Adenocarcinoma; qPCR, quantitative real-time Polymerase Chain Reaction; ROS, Reactive Oxygen Species; SOD1, Superoxide Dismutase 1; si qi, Four Properties; STAT3, Signal Transducer and Activator of Transcription 3; SAs, Structurally ordered Aggregates; Sox2, Sex Determining Region Y-Box 2; TAS2R, Taste 2 Receptor; TLR4, Toll-Like Receptor 4; TRPM5, Transient Receptor Potential Cation Channel Subfamily M Member 5; TRPV1, Transient Receptor Potential Vanilloid 1; TCMSP, Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform; TCM, Traditional Chinese medicine; TEAS, transcutaneous electrical acupoint stimulation; VEGF, Vascular Endothelial Growth Factor; wu wei, Five Flavors; XIAP, X-Linked Inhibitor of Apoptosis Protein.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare no competing financial or personal interests that could influence the work reported in this paper.

References

1. Lu F-J, Ding L-Q, Cao S-J, Zhang D-Q, Zhang B-L, Qiu F. [Chemistry and biology research on bitter-taste Chinese materia medica with function of regulating glycolipid metabolism]. *Zhongguo Zhong Yao Za Zhi*. 2018;43(19):3834–3840. Catalan. doi:10.19540/j.cnki.cjcmm.20180709.006
2. Zhu Y, Liu Y, Qian Y, et al. Antimetastatic effects of Celastrus orbiculatus on human gastric adenocarcinoma by inhibiting epithelial-mesenchymal transition and NF-κB/snail signaling pathway. *Integr Cancer Ther*. 2015;14(3):271–281. doi:10.1177/1534735415572880
3. Tuan NQ, Lee DH, Oh J, et al. Inhibition of proliferation of vascular smooth muscle cells by cucurbitanes from Momordica charantia. *J Nat Prod*. 2017;80(7):2018–2025. doi:10.1021/acs.jnatprod.7b00151
4. Panchal K, Nihalani B, Oza U, Panchal A, Shah B. Exploring the mechanism of action bitter melon in the treatment of breast cancer by network pharmacology. *World J Exp Med*. 2023;13(5):142–155. doi:10.5493/wjem.v13.i5.142
5. Li SY, Shi CJ, Fu WM, Zhang JF. Berberine inhibits tumour growth in vivo and in vitro through suppressing the lincROR-Wnt/β-catenin regulatory axis in colorectal cancer. *J Pharm Pharmacol*. 2023;75(1):129–138. doi:10.1093/jpp/rgac067
6. Yan Z, Yu H, Zhang L, et al. Network pharmacology and bioinformatics analysis identify potential therapeutic effects of berberine on colon cancer complicated with radiation enteritis. *Acupuncture Herbal Med*. 2024;4(4):500–512. doi:10.1097/HM9.0000000000000121
7. Wang XZ, Xia L, Zhang XY, et al. The multifaceted mechanisms of Paeoniflorin in the treatment of tumors: state-of-the-Art. *Biomed Pharmacother*. 2022;149:112800. doi:10.1016/j.biopha.2022.112800
8. Huang R, Zhang L, Jin J, et al. Bruceine D inhibits HIF-1α-mediated glucose metabolism in hepatocellular carcinoma by blocking ICAT/β-catenin interaction. *Acta Pharm Sin B*. 2021;11(11):3481–3492. doi:10.1016/j.apsb.2021.05.009
9. Niu J, Wang J, Zhang Q, Zou Z, Ding Y. Cinobufagin-induced DNA damage response activates G(2)/M checkpoint and apoptosis to cause selective cytotoxicity in cancer cells. *Cancer Cell Int*. 2021;21(1):446. doi:10.1186/s12935-021-02150-0
10. Wei Y, Wang Y, Zang A, et al. Inducible T-cell co-stimulators regulate the proliferation and invasion of human hepatocellular carcinoma HepG2 cells. *Biol Res*. 2018;51(1):2. doi:10.1186/s40659-017-0150-7
11. Tian G, Chen J, Luo Y, Yang J, Gao T, Shi J. Ethanol extract of *Ligustrum lucidum Ait*. leaves suppressed hepatocellular carcinoma in vitro and in vivo. *Cancer Cell Int*. 2019;19(1):246. doi:10.1186/s12935-019-0960-5
12. Guo W, Liu S, Ju X, et al. The antitumor effect of hinesol, extract from *Atractylodes lancea* (*Thunb*.) *DC*. by proliferation, inhibition, and apoptosis induction via MEK/ERK and NF-κB pathway in non–small cell lung cancer cell lines A549 and NCI-H1299. *J Cell Biochem*. 2019;120 (11):18600–18607. doi:10.1002/jcb.28696
13. Arshi A, Hosseini SM, Hosseini FSK, et al. The anti-cancer effect of amygdalin on human cancer cell lines. *Mol Biol Rep*. 2019;46(2):2059–2066. doi:10.1007/s11033-019-04656-3
14. Chen T, Li B, Qiu Y, Qiu Z, Qu P. Functional mechanism of Ginsenosides on tumor growth and metastasis. *Saudi J Biol Sci*. 2018;25(5):917–922. doi:10.1016/j.sjbs.2018.01.012
15. Liu D, Jin X, Yu G, et al. Oleanolic acid blocks the purine salvage pathway for cancer therapy by inactivating SOD1 and stimulating lysosomal proteolysis. *Mol Ther Oncolytics*. 2021;23:107–123. doi:10.1016/j.omto.2021.08.013
16. Yang K-D, Zhang X, Shao M-C, Wang L-N. Aconite aqueous extract inhibits the growth of hepatocellular carcinoma through CCL2-dependent enhancement of natural killer cell infiltration. *J Integr Med*. 2023;21(6):575–583. doi:10.1016/j.joim.2023.10.002
17. Du J, Lu X, Long Z, et al. In vitro and in vivo anticancer activity of aconitine on melanoma cell line B16. *Molecules*. 2013;18(1):757–767. doi:10.3390/molecules18010757
18. Subhawa S, Chewonarin T, Banjerdpongchai R. The effects of *Houttuynia cordata* thunb and *Piper ribesioides* wall extracts on breast carcinoma cell proliferation, migration, invasion and apoptosis. *Molecules*. 2020;25(5). doi:10.3390/molecules25051196
19. Elmore S. Apoptosis: a review of programmed cell death. *Toxicol Pathol*. 2007;35(4):495–516. doi:10.1080/01926230701320337
20. Telang NT, Nair HB, Wong GYC. Growth inhibitory efficacy of Cornus officinalis in a cell culture model for triple-negative breast cancer. *Oncol Lett*. 2019;17(6):5261–5266. doi:10.3892/ol.2019.10182
21. Shanmugam MK, Dai X, Kumar AP, Tan BK, Sethi G, Bishayee A. Ursolic acid in cancer prevention and treatment: molecular targets, pharmacokinetics and clinical studies. *Biochem Pharmacol*. 2013;85(11):1579–1587. doi:10.1016/j.bcp.2013.03.006
22. Liu F, Wang JG, Li Y, Wang SY, Wu YP, Xi SM. Antitumor effect and mechanism of Gecko on human esophageal carcinoma cell lines in vitro and xenografted sarcoma 180 in Kunming mice. *World J Gastroenterol*. 2008;14(25):3990–3996. doi:10.3748/wjg.14.3990
23. Liu S, Xu M, Zhu C, Zhao Q, Zhou F. Taste receptor T1R1/T1R3 promotes the tumoricidal activity of hepatic CD49a(+) CD49b(-) natural killer cells. *Eur J Immunol*. 2018;48(12):2031–2041. doi:10.1002/eji.201847688
24. Zopun M, Liszt KI, Stoeger V, et al. Human sweet receptor T1R3 is functional in human gastric parietal tumor cells (HGT-1) and modulates cyclamate and acesulfame K-induced mechanisms of gastric acid secretion. *J Agric Food Chem*. 2018;66(19):4842–4852. doi:10.1021/acs.jafc.8b00658
25. Ware AW, Harris JJ, Slatter TL, Cunliffe HE, McDonald FJ. The epithelial sodium channel has a role in breast cancer cell proliferation. *Breast Cancer Res Treat*. 2021;187(1):31–43. doi:10.1007/s10549-021-06133-7

26. Zhai K, Liskova A, Kubatka P, Büsselberg D. Calcium entry through TRPV1: a potential target for the regulation of proliferation and apoptosis in cancerous and healthy cells. *Int J Mol Sci*. 2020;21(11). doi:10.3390/ijms21114177
27. Gao N, Yang F, Chen S, Wan H, Zhao X, Dong H. The role of TRPV1 ion channels in the suppression of gastric cancer development. *J Exp Clin Cancer Res*. 2020;39(1):206. doi:10.1186/s13046-020-01707-7
28. Behrens M, Ziegler F. Structure-function analyses of human bitter taste receptors-where do we stand? *Molecules*. 2020;25(19). doi:10.3390/molecules25194423
29. Facchini FA, Zaffaroni L, Minotti A, et al. Structure-activity relationship in monosaccharide-based toll-like receptor 4 (TLR4) antagonists. *J Med Chem*. 2018;61(7):2895–2909. doi:10.1021/acs.jmedchem.7b01803
30. Behrens M, Gu M, Fan S, Huang C, Meyerhof W. Bitter substances from plants used in traditional Chinese medicine exert biased activation of human bitter taste receptors. *Chem Biol Drug Des*. 2018;91(2):422–433. doi:10.1111/cbdd.13089
31. Veale EL, Mathie A. Aristolochic acid, a plant extract used in the treatment of pain and linked to Balkan endemic nephropathy, is a regulator of K2P channels. *Br J Pharmacol*. 2016;173(10):1639–1652. doi:10.1111/bph.13465
32. Li P, Ren K, Liang YY, Liu JK, Liang ZW, Zhang YF. Aloin promotes cell apoptosis by targeting HMGB1-TLR4-ERK axis in human melanoma cells. *Excli J*. 2020;19:641–651.
33. Ji M, Su X, Su X, et al. Identification of novel compounds for human bitter taste receptors. *Chem Biol Drug Des*. 2014;84(1):63–74. doi:10.1111/cbdd.12293
34. Harmon CP, Deng D, Breslin PAS. Bitter taste receptors (T2Rs) are sentinels that coordinate metabolic and immunological defense responses. *Curr Opin Physiol*. 2021;20:70–76. doi:10.1016/j.cophys.2021.01.006
35. Tuzim K, Korolczuk A. Correction to: an update on extra-oral bitter taste receptors. *J Transl Med*. 2021;19(1):478. doi:10.1186/s12967-021-03137-1
36. Lossow K, Hübner S, Roudnitzky N, et al. Comprehensive analysis of mouse bitter taste receptors reveals different molecular receptive ranges for orthologous receptors in mice and humans. *J Biol Chem*. 2016;291(29):15358–15377. doi:10.1074/jbc.M116.718544
37. Zheng K, Lu P, Delpapa E, et al. Bitter taste receptors as targets for tocolytics in preterm labor therapy. *FASEB J*. 2017;31(9):4037–4052. doi:10.1096/fj.201601323RR
38. Duarte AC, Santos J, Costa AR, et al. Bitter taste receptors profiling in the human blood-cerebrospinal fluid-barrier. *Biochem Pharmacol*. 2020;177:113954. doi:10.1016/j.bcp.2020.113954
39. Sternini C. Taste receptors in the gastrointestinal tract. IV. Functional implications of bitter taste receptors in gastrointestinal chemosensing. *Am J Physiol Gastrointest Liver Physiol*. 2007;292(2):G457–461. doi:10.1152/ajpgi.00411.2006
40. Singh N, Shaik FA, Myal Y, Chelikani P. Chemosensory bitter taste receptors T2R4 and T2R14 activation attenuates proliferation and migration of breast cancer cells. *Mol Cell Biochem*. 2020;465(1–2):199–214. doi:10.1007/s11010-019-03679-5
41. Seo Y, Kim YS, Lee KE, Park TH, Kim Y. Anti-cancer stemness and anti-invasive activity of bitter taste receptors, TAS2R8 and TAS2R10, in human neuroblastoma cells. *PLoS One*. 2017;12(5):e0176851. doi:10.1371/journal.pone.0176851
42. Carey RM, McMahon DB, Miller ZA, et al. T2R bitter taste receptors regulate apoptosis and may be associated with survival in head and neck squamous cell carcinoma. *Mol Oncol*. 2022;16(7):1474–1492. doi:10.1002/1878-0261.13131
43. Bi S, Zhu J, Huang L, et al. Comprehensive analysis of the function and prognostic value of TAS2Rs family-related genes in colon cancer. *Int J Mol Sci*. 2024;25(13). doi:10.3390/ijms25136849
44. Martin LTP, Nachtigal MW, Selman T, et al. Bitter taste receptors are expressed in human epithelial ovarian and prostate cancers cells and noscapine stimulation impacts cell survival. *Mol Cell Biochem*. 2019;454(1–2):203–214. doi:10.1007/s11010-018-3464-z
45. Liu L, Zhu Q, Du H, Shi C, Gu M, Li X. New values of a type 2 taste receptor TAS2R14 in thyroid cancer. *Acta Biochim Biophys Sin*. 2022;54(4):587–589. doi:10.3724/abbs.2022026
46. Stern L, Giese N, Hackert T, et al. Overcoming chemoresistance in pancreatic cancer cells: role of the bitter taste receptor T2R10. *J Cancer*. 2018;9(4):711–725. doi:10.7150/jca.21803
47. Gaida MM, Mayer C, Dapunt U, et al. Expression of the bitter receptor T2R38 in pancreatic cancer: localization in lipid droplets and activation by a bacteria-derived quorum-sensing molecule. *Oncotarget*. 2016;7(11):12623–12632. doi:10.18632/oncotarget.7206
48. Fu Y, Zhu F, Ma Z, et al. *Physalis alkekengi* var. *franchetii* extracts exert antitumor effects on non-small cell lung cancer and multiple myeloma by inhibiting STAT3 signaling. *Onco Targets Ther*. 2021;14:301–314. doi:10.2147/ott.S282334
49. Lv XJ, Zhao LJ, Hao YQ, et al. Schisandrin B inhibits the proliferation of human lung adenocarcinoma A549 cells by inducing cycle arrest and apoptosis. *Int J Clin Exp Med*. 2015;8(5):6926–6936.
50. Chen MC, Wu SV, Reeve JR Jr, Rozengurt E. Bitter stimuli induce Ca2+ signaling and CCK release in enteroendocrine STC-1 cells: role of L-type voltage-sensitive Ca2+ channels. *Am J Physiol Cell Physiol*. 2006;291(4):C726–739. doi:10.1152/ajpcell.00003.2006
51. Hazafa A, Rehman KU, Jahan N, Jabeen Z. The role of polyphenol (Flavonoids) compounds in the treatment of cancer cells. *Nutr Cancer*. 2020;72(3):386–397. doi:10.1080/01635581.2019.1637006
52. Sun M, Han J, Duan J, et al. Novel antitumor activities of Kushen flavonoids in vitro and in vivo. *Phytother Res*. 2007;21(3):269–277. doi:10.1002/ptr.2066
53. Zhang XL, Cao MA, Pu LP, et al. A novel flavonoid isolated from Sophora flavescens exhibited anti-angiogenesis activity, decreased VEGF expression and caused G0/G1 cell cycle arrest in vitro. *Pharmazie*. 2013;68(5):369–375.
54. Zhu J, Zhang H, Zhu Z, et al. Effects and mechanism of flavonoids from Astragalus complanatus on breast cancer growth. *Naunyn Schmiedebergs Arch Pharmacol*. 2015;388(9):965–972. doi:10.1007/s00210-015-1127-0
55. Park S, Bazer FW, Lim W, Song G. The O-methylated isoflavone, formononetin, inhibits human ovarian cancer cell proliferation by sub G0/G1 cell phase arrest through PI3K/AKT and ERK1/2 inactivation. *J Cell Biochem*. 2018;119(9):7377–7387. doi:10.1002/jcb.27041
56. Liang C, Jiang J, Li J, et al. The anti-melanoma roles and mechanisms of tricholoma isoflavone derivative CA028. *NPJ Sci Food*. 2025;9(1):4. doi:10.1038/s41538-025-00370-6
57. Škubník J, Pavlíčková VS, Ruml T, Rimpelová S. Vincristine in combination therapy of cancer: emerging trends in clinics. *Biology*. 2021;10(9). doi:10.3390/biology10090849
58. Zhang Y, Zhang H, Yu P, et al. Effects of matrine against the growth of human lung cancer and hepatoma cells as well as lung cancer cell migration. *Cytotechnology*. 2009;59(3):191–200. doi:10.1007/s10616-009-9211-2

59. Frederich M, Bentires-Ali M, Tits M, Angenot L, Heinen E, De Pauw-Gillet MC. Apoptosis induction in human cancer cells by sungucine from Strychnos icaja root. *Naunyn Schmiedebergs Arch Pharmacol*. 2003;367(3):260–265. doi:10.1007/s00210-003-0691-x
60. Guo B, Zhang T, Su J, Wang K, Li X. Oxymatrine targets EGFR(p-Tyr845) and inhibits EGFR-related signaling pathways to suppress the proliferation and invasion of gastric cancer cells. *Cancer Chemother Pharmacol*. 2015;75(2):353–363. doi:10.1007/s00280-014-2651-1
61. Liu R, Peng J, Wang H, et al. Oxysophocarpine retards the growth and metastasis of oral squamous cell carcinoma by targeting the Nrf2/HO-1 axis. *Cell Physiol Biochem*. 2018;49(5):1717–1733. doi:10.1159/000493615
62. Wang A, Wang M, Pang Q, et al. Lily extracts inhibit the proliferation of gastric carcinoma SGC-7901 cells by affecting cell cycle progression and apoptosis via the upregulation of caspase-3 and Fas proteins, and the downregulation of FasL protein. *Oncol Lett*. 2018;16(2):1397–1404. doi:10.3892/ol.2018.8806
63. Xiao X, Yang M, Xiao J, et al. Paris Saponin II suppresses the growth of human ovarian cancer xenografts via modulating VEGF-mediated angiogenesis and tumor cell migration. *Cancer Chemother Pharmacol*. 2014;73(4):807–818. doi:10.1007/s00280-014-2408-x
64. Kim JY, Choi HY, Kim HM, Choi JH, Jang DS. A novel cytotoxic steroidal saponin from the roots of *Asparagus cochinchinensis*. *Plants*. 2021;10 (10). doi:10.3390/plants10102067
65. Zhang RS, Liu YY, Zhu PF, Jin Q, Dai Z, Luo XD. Furostanol Saponins from *Asparagus cochinchinensis* and Their Cytotoxicity. *Nat Prod Bioprospect*. 2021;11(6):651–658. doi:10.1007/s13659-021-00321-0
66. Chi XJ, Meng JJ, Lin CY, et al. Mangiferin inhibits human lung adenocarcinoma by suppressing MiR-27b and MiR-92a. *Evid Based Complement Alternat Med*. 2021;2021:2822950. doi:10.1155/2021/2822950
67. Lin YS, Tsai KL, Chen JN, Wu CS. Mangiferin inhibits lipopolysaccharide-induced epithelial-mesenchymal transition (EMT) and enhances the expression of tumor suppressor gene PER1 in non-small cell lung cancer cells. *Environ Toxicol Int J*. 2020;35(10):1070–1081. doi:10.1002/tox.22943
68. Veerabhadrappa B, Subramanian S, Sudharshan SJ, Dyavaiah M. Evaluating the genetic basiss of anti-cancer property of Taxol in *Saccharomyces cerevisiae* model. *FEMS Microbiol Lett*. 2021;368(13). doi:10.1093/femsle/fnab077
69. Wang YY, Lv YF, Lu L, Cai L. Oridonin inhibits mTOR signaling and the growth of lung cancer tumors. *Anticancer Drugs*. 2014;25 (10):1192–1200. doi:10.1097/cad.0000000000000154
70. Wang BY, Cao J, Chen JW, Liu QY. Triptolide induces apoptosis of gastric cancer cells via inhibiting the overexpression of MDM2. *Med Oncol*. 2014;31(11):270. doi:10.1007/s12032-014-0270-7
71. Wu J, Li QQ, Zhou H, et al. Selective tumor cell killing by triptolide in p53 wild-type and p53 mutant ovarian carcinomas. *Med Oncol*. 2014;31 (7):14. doi:10.1007/s12032-014-0014-8
72. Zhu L, Li J, Wang ZQ, et al. Treatment of moderate-to-severe pain in hepatocellular carcinoma with transcutaneous electrical acupoint stimulation: a randomized controlled trial. *J Pain Res*. 2024;17:1583–1594. doi:10.2147/jpr.S456874
73. Chen L-X, Yan F. Clinical study on auricular point sticking plus Western medicine for moderate gastric cancer pain. *J Acupunct Tuina Sci*. 2020;18 (4):276–280. doi:10.1007/s11726-020-1188-6
74. Huang D, Tang Z, Pu X, Wang T, Gao F, Li C. A novel cabazitaxel liposomes modified with ginsenoside Rk1 for cancer targeted therapy. *Acupuncture Herbal Med*. 2024;4(1):113–121. doi:10.1097/HM9.0000000000000096
75. Sternini C, Rozengurt E. Bitter taste receptors as sensors of gut luminal contents. *Nat Rev Gastroenterol Hepatol*. 2025;22(1):39–53. doi:10.1038/s41575-024-01005-z
76. Yu S, Wang S, Huang S, et al. Radix et Rhizoma Ginseng chemoprevents both initiation and promotion of cutaneous carcinoma by enhancing cell-mediated immunity and maintaining redox homeostasis. *J Ginseng Res*. 2020;44(4):580–592. doi:10.1016/j.jgr.2019.05.004
77. Fang C, Wang Y, Pan Z. Formation of self-assembly aggregates in traditional Chinese medicine decoctions and their application in cancer treatments. *RSC Adv*. 2025;15(7):5476–5506. doi:10.1039/d4ra07212j
78. Sonkin D, Thomas A, Teicher BA. Cancer treatments: past, present, and future. *Cancer Genet*. 2024;286-287:18–24. doi:10.1016/j.cancergen.2024.06.002
79. Liu H. Effect of traditional medicine on clinical cancer. *Biomed J Scientific Techn Res*. 2020;30(4). doi:10.26717/bjstr.2020.30.004979
80. McBrearty N, Bahal D, Platero S. Fast-tracking drug development with biomarkers and companion diagnostics. *J Cancer Metastatis Treat*. 2024. doi:10.20517/2394-4722.2023.134
81. Joshia RM, Telang B, Sonic G, Khalifea A. overview of perspectives on cancer,_newer. *Oncol Transl Med*. 2024;10. doi:10.1097/ot9.0000000000000039

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