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REVIEW

The Crosstalk Between Epithelial-Mesenchymal Transition and Anoikis Resistance: A New Perspective of Traditional Chinese Medicine to Prevent Tumor Metastasis

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Abstract: Tumour metastasis is a significant factor that threatens human health and life. Current research has shown that Traditional Chinese Medicine (TCM) can inhibit epithelial-mesenchymal transition (EMT) and restore the sensitivity of tumour cells to anoikis by influencing tumour metabolism, the extracellular matrix, transcription factors, related signalling pathways, and non-coding RNA. This review summarises 46 types of TCM (including single herb extracts, compounds, and formulations) that may reduce tumour recurrence and metastasis rates in cancer treatment. The findings indicate that TCM regulates EMT and anoikis processes by modulating the Wnt/β-catenin, TGF-β, and PI3K/AKT signalling pathways, thereby affecting the extracellular matrix, apoptosis, and metabolic reprogramming. TCM targets molecular mechanisms to construct signal pathway networks to regulate EMT and anoikis, ultimately achieving the inhibition of tumour metastasis. This discovery provides new insights for the application of TCM in future cancer treatment.

Keywords: traditional chinese medicine, tumor metastasis, epithelial-mesenchymal transition, anoikis resistance

Introduction

Approximately 90% of cancer-related deaths are attributable to the dissemination of primary tumor cells to distant sites beyond their original location.[1] These malignant cells disseminate via the lymphatic system, bloodstream, or other bodily compartments, eventually colonizing remote tissues where they proliferate. This process, known as metastasis, represents the terminal and most lethal stage of cancer progression.[2] During metastatic dissemination, the primary tumor invades adjacent tissues and profoundly remodels the surrounding stromal microenvironment. Neoplastic cells subsequently enter the circulation via mechanisms of invasion and intravasation. Upon entry into the bloodstream, tumor cells must adapt to and survive within the fluid, suspension environment.[3] These circulating tumor cells then extravasate into distant organs, where they establish micrometastases that may eventually progress to overt metastatic lesions.[4] A prerequisite for successful metastasis is enhanced cellular motility and invasiveness, which largely depends on dynamic interactions between tumor cells and the stromal components, as well as the induction of epithelial-mesenchymal transition (EMT) in tumor cells.[5] EMT is characterized by the loss of epithelial features—such as apical-basal polarity and tight intercellular junctions—and the acquisition of mesenchymal traits, including increased motility and invasiveness.[6] Importantly, the acquisition of EMT characteristics alone does not directly result in metastasis. Tumor cells at the primary site are often anchored to adjacent cells and the extracellular matrix (ECM), and their detachment can trigger a specific form of

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programmed cell death known as anoikis. Therefore, for tumor cells to survive in the circulation and establish secondary lesions, they must acquire resistance to anoikis.[7] This resistance is recognized as a hallmark of metastatic potential and is closely linked to tumor cell invasion, intravasation, and distant colonization.[8] Recent studies have demonstrated that anoikis resistance is a pivotal determinant of the survival of detached cancer cells during metastasis, and its molecular regulation is closely intertwined with EMT. This process is further modulated by multiple microenvironmental adaptation strategies, including redox homeostasis, autophagy, immune evasion, and maintenance of stemness, while the metabolic and epigenetic plasticity associated with EMT can drive cancer cell survival under therapeutic intervention through an EMT–anoikis–metabolism crosstalk, ultimately promoting metastatic dissemination.[9–12] An increasing body of evidence suggests that EMT not only facilitates metastasis but also confers survival advantages by helping tumor cells evade apoptosis induced by external stressors, thereby enhancing cellular viability.[13] Furthermore, EMT may contribute to the acquisition of anoikis resistance by altering the biochemical composition and mechanical properties of the ECM.[14] These findings point toward a mechanistic interplay between EMT and anoikis resistance in promoting metastasis. However, the precise molecular crosstalk between these processes remains to be fully elucidated.

With advances in molecular biology, increasing evidence has elucidated the molecular targets and mechanisms by which Traditional Chinese Medicine (TCM) inhibits tumor metastasis.[15] An increasing number of studies have consistently shown that the combination of TCM treatment with chemotherapy drugs for tumors can reduce the chances of tumor recurrence and metastasis, prolong the survival period of patients, and improve their quality of life.[16–19] Notably, most active components of TCM are derived from natural plants, which exhibit favorable safety profiles, low toxicity, and good tolerability at clinical doses.[20] In contrast to single-target agents, TCM possesses unique advantages in simultaneously regulating multiple signaling pathways and molecular targets, making it highly promising for intervening in complex metastatic networks.[21,22] Additionally, targeted anti-tumor drugs often impose substantial economic burdens on patients, whereas TCM is more economically accessible and holds great potential for widespread development and clinical translation. In this review, we systematically summarise cumulatively the research findings, which investigate the inhibitory effects of TCM on tumor metastasis, particularly through modulation of EMT and anoikis. We aim to elucidate the potential mechanisms underlying the crosstalk between EMT and anoikis in the context of TCM intervention, and discuss these findings in light of the current body of relevant literature (as illustrated in Figure 1).

Crosstalk Mechanism of EMT and Anoikis

The Link Between EMT and Anoikis: ECM Is the Key

The ECM refers to the non-cellular component of tissues that not only provides structural support for resident cells but also constitutes a critical part of their surrounding microenvironment.[23] Although the physical properties and structural composition of the ECM differ across tissue types, its core functions remain highly conserved, including roles in cell adhesion, intercellular communication, and regulation of cell differentiation. Emerging studies have identified that the ECM appears to be a key link between EMT and anoikis, which is mediated primarily through structural and compositional changes in the ECM.[24] EMT is characterized by the downregulation of epithelial markers such as cytokeratins and E-cadherin, and the upregulation of mesenchymal markers including N-cadherin, vimentin, and fibronectin.[25] This shift in gene expression results in reduced intercellular adhesion and promotes the expression of proteolytic enzymes—particularly matrix metalloproteinases (MMPs), along with fibrinolytic enzymes and histones—that contribute to ECM degradation.[26] Moreover, ECM components and signaling molecules altered during EMT, such as fibronectin and vimentin, can engage specific cell surface receptors to activate downstream signaling pathways that promote resistance to anoikis. This, in turn, affects cellular adhesion, migration, and survival.[7] Importantly, this regulatory relationship is not unidirectional. In tumor cells that have acquired anoikis resistance, the downregulation of epithelial adhesion molecules such as E-cadherin and β-catenin further facilitates the induction of EMT (as illustrated in Figure 2).[27]

Research has demonstrated that EMT is tightly regulated by a cohort of transcription factors (TFs), including zinc finger E-box binding homeobox 1 (ZEB1), ZEB2, Snail, Slug, and Twist.[28] These TFs contribute to anoikis resistance primarily through two mechanisms: the disruption of intercellular junctions and the inhibition of apoptotic signaling pathways. Several of these transcription factors—such as Snail, Slug, ZEB1, and ZEB2 (also known as smad interacting

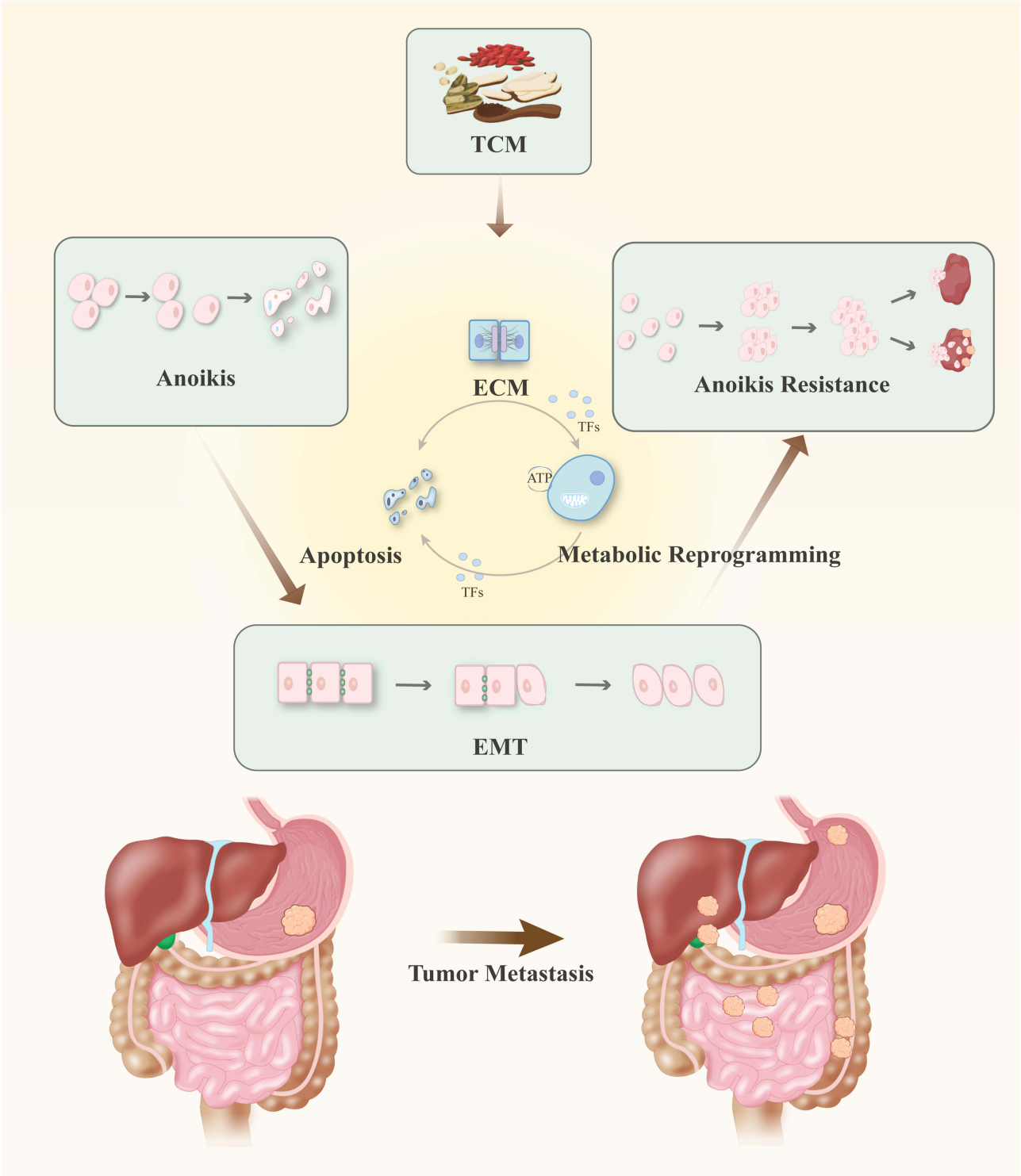

Figure 1 Visual Summary. Schematic representation of the interaction mechanism of TCM targeting EMT and anoikis resistance to interfere with tumor metastasis.

protein 1 (SIP1))—act as direct repressors of E-cadherin by binding to E-box elements within the E-cadherin promoter region.[29,30] In contrast, indirect repression of E-cadherin is mediated by other TFs including Twist1, Twist2, homeobox proteins (e.g., goosecoid (GSC) and SIX homeobox 1 (SIX1)), E2.2, and the forkhead box protein C2 (FOXC2).[31,32] Interestingly, although Twist proteins are typically categorized as indirect repressors, studies have shown that they are also capable of directly binding to E-box2 and E-box3 on the E-cadherin promoter, thereby suppressing its

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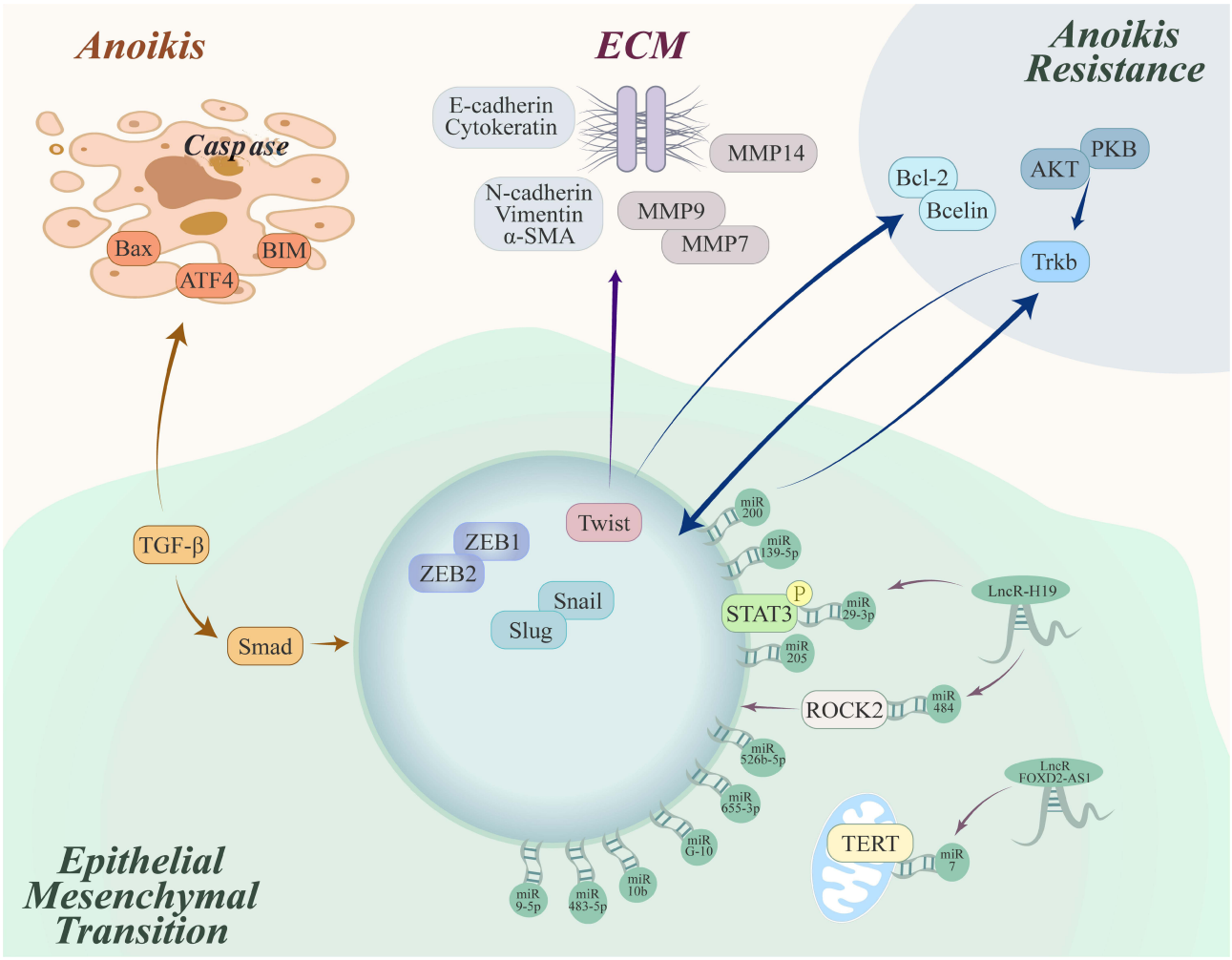

Figure 2 ECM-mediated EMT drives the anoikis-to-anoikis-resistance switch. ECM induces EMT through signal remodeling. The EMT transcription factors, TGF-β, non-coding RNAs and integrin pathways synergistically promote cell invadopodia anoikis resistance, forming a bidirectional regulatory loop to drive tumor invasion and metastasis.

transcription.[33] In addition to repressing epithelial markers, Twist proteins also promote the expression of mesenchymal markers such as fibronectin, vimentin, α-SMA, and N-cadherin.[34] Moreover, Twist facilitates the formation of invasive pseudopodia enriched with filamentous actin, which are instrumental in directing the secretion of matrix-degrading enzymes, including MMP7, MMP9, and MMP14. These MMPs degrade components of the extracellular matrix and basement membrane, thereby enhancing tumor cell invasion and metastatic potential.[26]

The regulatory role of some signaling pathways on ECM was also observed by us. Among them, the cytokine transforming growth factor-β (TGF-β) is widely recognized as a central inducer of both physiological and pathological EMT, particularly within the context of cancer. In malignant cells, the TGF-β/Smad signaling pathway, along with the transcription factor ras responsive element binding protein 1 (RREB1), has been shown to directly upregulate the expression of Snail, a key EMT regulator. This upregulation promotes the activation of fibroblasts and contributes to the development of fibrosis within the tumor microenvironment. The resulting fibrotic milieu facilitates the production of ECM-associated fibrotic mediators that support tumor progression and metastasis.[35] Mechanistically, TGF-β ligands form homodimers or heterodimers that bind to their cognate type II and type I transmembrane receptors. Upon ligand binding, the type II receptor phosphorylates the type I receptor, thereby activating its kinase activity. The activated type I receptor subsequently phosphorylates receptor-regulated Smad proteins, which translocate into the nucleus and function as transcription factors to modulate the expression of target genes.[36] The TGF-β/Smad signaling axis has been extensively

implicated in fibrotic responses across a range of pathological conditions.[37] In addition, TGF-β signaling regulates the expression of MMPs, further contributing to ECM remodeling and degradation, thereby facilitating tumor invasion and metastasis.[38]

Non-coding RNAs are also crucial regulatory parts in the EMT and anoikis processes, and they are usually indirectly regulated through TFs and pathways. As a type of non-coding RNA, microRNA (miRNA) regulates the expression of target genes mainly by binding to the messenger RNA (mRNA) of target genes and affecting their stability and translation activity.[39] Several miRNAs have been reported to influence anoikis resistance via modulation of EMT. These include miR-9-5p, miR-10b, miR-139-5p, miR-483-5p, miR-526b-5p, miR-655-3p, and miR-G-10.[40] Of particular interest is the miR-200 family—comprising miR-200a, miR-200b, and miR-200c—which plays a pivotal role in maintaining epithelial cell characteristics by repressing the expression of EMT-inducing transcription factors ZEB1 and ZEB2.[41] Notably, miR-200c has been shown to modulate EMT in both breast and endometrial cancers and to regulate anoikis resistance via targeting tyrosine kinase receptor B (TrkB).[42] In addition to miRNAs, lncRNAs also play an important role, and the involvement of these lncRNAs in EMT regulation of anoikis is usually achieved by modulating miRNAs or related signaling pathways.

For instance, long noncoding RNA FOXD2 adjacent opposite strand RNA 1 (lncRNA-FOXD2-AS1) targets miR-7-5p to mediate telomerase reverse transcriptase and promotes anchorage-independent cell growth, whereas lncRNA-H19 facilitates EMT by sequestering miR-29-3p and miR-484, which normally suppress the expression of signal transducer and activator of transcription 3 (STAT3) and Rho-associated coiled-coil containing protein kinase 2 (ROCK2), respectively.[43] In thyroid cancer, knockdown of long noncoding RNA small nucleolar RNA host gene 12 (lncRNA-SNHG12) has been shown to inactivate Wnt/β-catenin signaling, thus inhibiting tumor cell migration.[44] In addition, other lncRNAs involved are long noncoding RNA HOX antisense intergenic RNA (lncRNA-HOTAIR), long noncoding RNA LEF1 antisense RNA 1 (lncRNA-LEF1-AS1), long noncoding RNA maternally expressed gene 3 (lncRNA-MEG3), long noncoding RNA nuclear paraspeckle assembly transcript 1 (lncRNA-NEAT1), and long noncoding RNA TINCR Ubiquitin Domain Containing (lncRNA -TINCR).[40]

The role of the integrin pathway is also of interest. Integrins are a family of transmembrane glycoprotein receptors composed of at least 25 α-subunits and 11 β-subunits, which assemble into more than 20 distinct heterodimeric integrin complexes through non-covalent interactions.[45] Integrins mediate EMT progression in tumor cells via multiple signaling cascades, including FAK, PI3K/AKT, and mitogen-activated protein kinase (MAPK) pathways, and EMT itself can further promote the upregulation of specific integrin subtypes.[46] This bidirectional regulation contributes to enhanced tumor cell plasticity and metastatic potential. In normal epithelial tissues, cells predominantly express the collagen receptor α2β1 and the laminin receptors α3β1 and α6β1. In contrast, hyperproliferative epithelial cells and various carcinomas frequently exhibit overexpression of integrins such as αvβ5 and αvβ6. Notably, αvβ6 is strongly upregulated in dermatofibrosarcoma and other aggressive tumors. These changes in integrin expression patterns are closely related to the enhanced ability of cell invasion and the increased resistance of cells to detachment from the adherent state, thereby facilitating the survival of tumors during the metastasis process.[47]

EMT and Anoikis: Involvement of Apoptotic Signaling

Mechanisms of anoikis include regulation of the expression of Bcl-2 and Bax family-related genes, and activation of the caspase family (as illustrated in Figure 3).[48] Bcl-2 serves as a principal anti-apoptotic protein, functioning to preserve mitochondrial membrane integrity and thereby prevent apoptosis.[49] In contrast, Bax, a pro-apoptotic member of the same family, promotes mitochondrial membrane permeabilization and is primarily localized to the mitochondrial outer membrane.[50] In the case of esophageal squamous cell carcinoma (ESCC), Twist1 has been shown to inhibit apoptosis by upregulating Bcl-2 and downregulating Bax, thereby contributing to anoikis resistance.[51] Another critical pro-apoptotic regulator is Bim, which initiates intrinsic apoptotic signaling and is often considered a key inducer of anoikis. EMT-associated TFs regulate these apoptosis-related proteins at the transcriptional level. For example, ZEB1 suppresses Bim expression by directly binding to its promoter region, thereby promoting anoikis resistance.[52] Similarly, silencing of Slug and Snail has been found to restore Bim expression and sensitize tumor cells to anoikis. Beyond gene regulation, these TFs also interfere with apoptotic signaling pathways, including the mitochondrial (intrinsic) pathway, and key

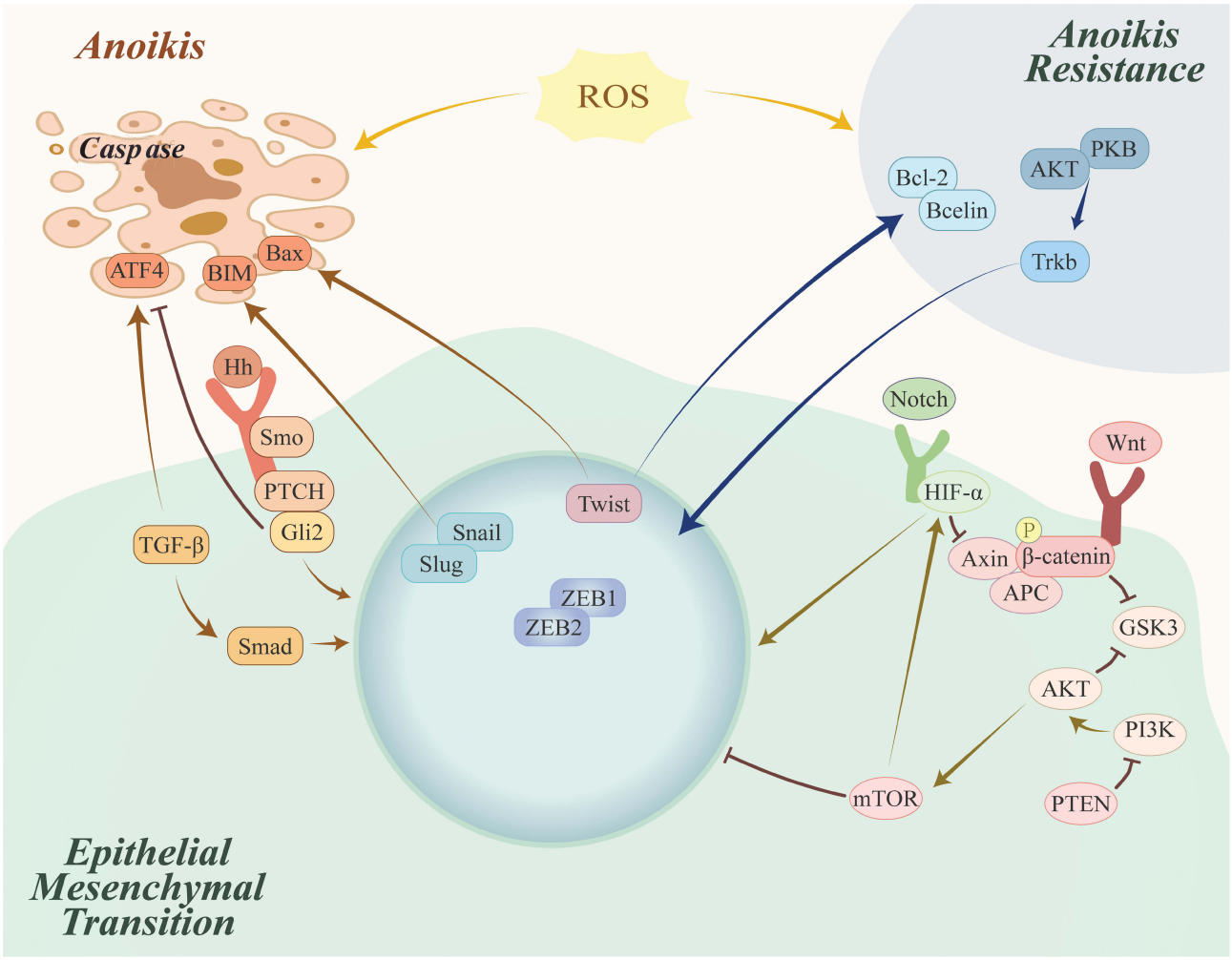

Figure 3 EMT Orchestrates Anoikis Resistance through Integrated Apoptotic Signaling and Metabolic Reprogramming. The schematic diagram illustrates the dual mechanism by which EMT mediates resistance to disintegrated apoptosis: by regulating apoptosis-related molecules such as Bcl-2 and Bax, the caspase family, as well as pathways such as TGF-β and PI3K/AKT to inhibit apoptosis, and simultaneously regulating metabolic reprogramming such as ROS levels and glycolysis, as well as molecules such as PDK4 and CEMIP, to help tumor cells adapt to the metabolic pressure after detachment from the ECM.

apoptotic effectors such as caspases.[53] A complex network of interconnected signaling pathways underlies the crosstalk between EMT and anoikis. Key pathways implicated include TGF-β, Wnt/β-catenin, PI3K/AKT, Notch, and Hedgehog. These pathways not only modulate EMT and ECM remodeling but also influence apoptosis by regulating EMT-TFs and apoptotic regulators. In breast cancer, for instance, TGF-β receptor 3 mediates anoikis through activating transcription factor 4 (ATF4).[54] The Wnt/β-catenin pathway contributes to anoikis resistance by inducing MMP expression and regulating TFs such as Snail, Slug, and Twist.[55] GLI is an effector protein of the Hedgehog signaling pathway, which plays a crucial part in cell adhesion and apoptosis.[56] It has been found that GLI2 increases anoikis resistance, whereas silencing of GLI, on the other hand, induces anoikis.[57] This may be attributed to Hedgehog-mediated upregulation of Snail and Slug.[58] Furthermore, in colorectal cancer (CRC), GLI2 has been reported to promote immune escape and anoikis resistance through TGF-β-mediated Hedgehog signaling.[27] Of particular interest are the PI3K/AKT and Notch signaling pathways, both of which can directly downregulate E-cadherin expression, distinguishing them from many other signal transduction mechanisms.[59] Activation of PI3K/AKT enhances Bcl-2 expression and inhibits anoikis, while Notch pathway activation promotes cell survival and proliferation under anchorage-independent conditions, thereby reinforcing anoikis resistance.[59,60]

EMT Regulates Anoikis: Interference with Metabolic Reprogramming

Several studies have identified the significance of metabolic reprogramming reconfiguration in the interplay between EMT and anoikis (as illustrated in Figure 3). Among the key metabolic regulators, reactive oxygen species (ROS) have been shown to play a dual and complex role in anoikis resistance, although the precise molecular mechanisms remain incompletely understood.[61] On one hand, physiological levels of ROS are essential for maintaining cell proliferation and adhesion. On the other hand, elevated ROS levels in cancer cells can promote anoikis resistance through the activation of chronic pro-survival signaling pathways.[62] In prostate cancer, the EMT transcription factor Snail has been implicated in the regulation of ROS production, and its overexpression is associated with increased ROS levels that contribute to anoikis resistance.[63] Under normal physiological conditions, detachment of epithelial cells from the ECM leads to impaired glucose transport, reduced adenosine triphosphate (ATP) production, and ultimately the induction of apoptosis. In contrast, metastatic cancer cells circumvent this energy stress through oncogene-driven metabolic adaptations, including enhanced glycolysis and fatty acid oxidation, which collectively support survival under anchorage-independent conditions.[61]

In human mammary epithelial cells, pyruvate dehydrogenase kinase 4 (PDK4)—upregulated via activation of estrogen receptor γ—induces a metabolic shift that reduces the conversion of pyruvate into acetyl-CoA, thereby suppressing glucose oxidation and enhancing anoikis resistance.[64] Another critical regulator is cell migration-inducing protein (CEMIP), which plays multiple roles in cell migration, invasion, and metabolic regulation. CEMIP promotes the production of pyruvate and lactate, supports intracellular ATP homeostasis, and enhances resistance to anoikis upon detachment from the ECM.[65] Mechanistically, CEMIP facilitates the translocation of protein kinase C alpha (PKCα) by inducing calcium release from the endoplasmic reticulum, which in turn promotes anoikis resistance and augments metastatic potential. At the plasma membrane, PKCα activates protective autophagy by disrupting the Bcl-2/Beclin-1 complex, enabling detached cells to survive under metabolic stress.[66]

The Mechanism by Which Dead Cells Promote Tumor Metastasis

In addition to the acquisition of anoikis resistance by tumor cells via EMT to survive upon matrix detachment, recent studies have revealed a critical reverse perspective: cells that die upon detachment from the primary site can themselves act as drivers that promote the invasion and migration of residual tumor cells. This bidirectional interaction renders the relationship between cell death and tumor progression far more complex (as illustrated in Figure 4). Anoikis is classically executed primarily through the apoptotic pathway, characterized by caspase-3 activation and loss of mitochondrial membrane potential.[67] However, recent studies have demonstrated that cells deprived of matrix adhesion can also undergo death via alternative pathways, including ferroptosis,[68] and autophagy-dependent cell death,[69] indicating that anoikis itself exhibits diversity in cell death modalities.

Studies have revealed that apoptotic tumor cells release S100a4-containing nuclear expulsion products into the extracellular space via a Padi4-mediated nuclear expulsion process. These products activate the advanced glycosylation End-Product specific receptor (RAGE) receptor on the surface of neighboring surviving cells, triggering the Erk signaling pathway and markedly enhancing the metastatic capacity of residual cancer cells.[70] Ferroptosis is an iron-dependent form of cell death driven by lipid peroxidation.[71] Recent research has established its double-edged role: on one hand, ferroptotic stress enhances tumor cell antigenicity and the release of danger signals, activating anti-tumor immune responses; on the other hand, lipid peroxides and damage-associated molecular patterns (DAMPs) released by ferroptotic cells can induce the polarization of tumor-associated macrophages toward an M2 phenotype and promote the formation of neutrophil extracellular traps (NETs). NETs have been shown to capture circulating tumor cells and facilitate their colonization.[72,73] A study in ovarian cancer reported that upon matrix detachment and spheroid formation, cells acquire ferroptosis resistance by efficiently utilizing iron ions to compensate for the loss of extracellular matrix.[74] During this process, iron metabolic reprogramming not only supports resistance to anoikis but also strengthens cell invasiveness. Autophagy, as a programmed cell death mechanism, plays an especially complex role in tumor metastasis. Studies in breast cancer have demonstrated that BR serine/threonine kinase 2 (BRSK2) associates with the Vps34-class III PI3K–Beclin-1–Autophagy Related 14 (ATG14) autophagy signaling complex, protecting cancer cells from anoikis and nutrient

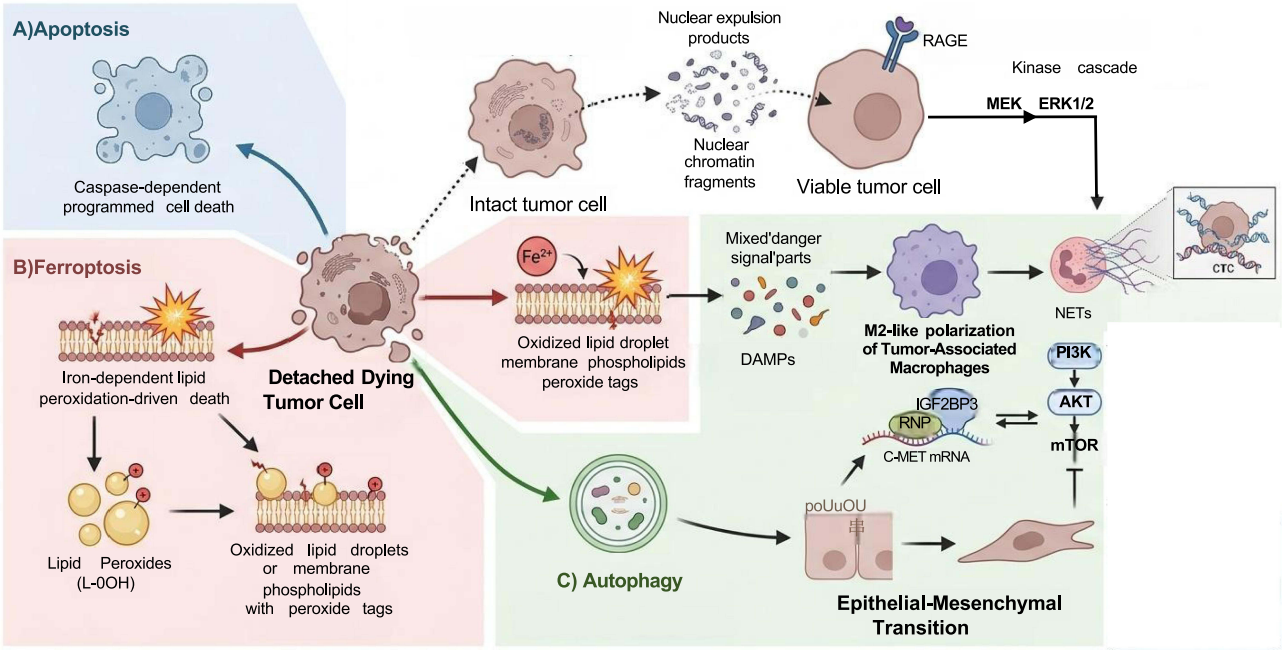

Figure 4 Diverse Cell Death Modalities and Their Bidirectional Crosstalk with Tumor Metastasis via Anoikis Regulation. The schematic diagram illustrates the diverse death modes of detached apoptosis (apoptosis, ferroptosis, autophagy-dependent cell death) and their bidirectional interaction with tumor metastasis, including the release of signals by dead cells promoting the invasion and migration of residual tumor cells, as well as the crosstalk among different death modes forming a positive feedback loop of "death-survival-metastasis".

deprivation. Inhibition of BRSK2 significantly reduces autophagic activity, enhances apoptosis, and suppresses metastasis.[75] Furthermore, autophagy promotes the EMT program by degrading epithelial markers such as E-cadherin. For instance, IGF2BP3, an m^6A-binding protein, promotes cap-independent translation of c-Met by binding to m^6A-modified sites on c-Met mRNA. This in turn regulates autophagy-mediated EMT via the c-Met/PI3K/AKT/mTOR pathway, driving metastasis in triple-negative breast cancer.[76] This finding uncovers an intricate regulatory network linking epigenetic modification, autophagy, and EMT. Notably, apoptosis, ferroptosis, and autophagy do not act independently but engage in an elaborate crosstalk network.[77] This crosstalk allows one form of cell death within the tumor microenvironment to amplify the pro-metastatic effects of other death modalities via signal integration, forming a positive feedback loop of "death–survival–metastasis".[78] Although multiple mechanisms by which dying cells promote metastasis have been uncovered, whether these findings are pan-cancer relevant and can be translated into universal therapeutic targets remains to be validated in larger tumor cohorts, across more cancer types, and in models that more closely recapitulate clinical settings.

Mechanisms of Inhibition of Tumour Metastasis by TCM

Research on single herb extracts and TCM formulations has shown that TCM can inhibit tumors by intervening in ECM, regulating apoptosis genes, controlling metabolism, and non-coding RNA. Table 1 summarizes detailed information on the active ingredients of single herbs, including their scientific names, traditional uses, effective dosages, routes of administration, and reported applications in oncology. Table 2 presents the composition and traditional therapeutic functions of classical TCM prescriptions, along with their documented roles in cancer treatment. Table 3 provides a comprehensive overview of how TCM influences tumor metastasis by targeting the mechanisms mentioned above, including EMT, anoikis resistance, and their upstream regulatory pathways.

Intervening in the ECM

TCM has been shown to inhibit tumor metastasis through multiple mechanisms, including indirect regulation of the ECM via signaling pathways and TFs, as well as direct remodeling of ECM structure and composition, thereby modulating

Table 1 TCM Understanding of Herbs and Compounds

Compounds Name	Herbs	Latin Name	Traditional use	Application in Tumor, Dosages and Routes of Administration	Reference (PMID)
Gallic acid	Wubeizi	*Rhus chinensis*	Heal sore and produce muscle	Pan-cancer, 210mg/kg, intraperitoneal injection	PMID:20564459 PMID: 31312226
Rosthorin A	Yinghuaxiangchacai	*Rabdosia amethystoides*	Dispersing wind wins dampness, dispersing stasis and relieving pain	NSCLC, 10 mg/kg, intraperitoneal injection	PMID:33065690
A Novel Aniline Derivative from Peganum harmala L.	Luotuopeng	*Peganum*	Dispel wind dampness, dispel depression	Pan-cancer, 20 mg/kg/d, intraperitoneal injection	PMID:33238864 PMID:29510387
Ethyl acetate extract of Biancaea sappan	Sumu	*Biancaea sappan*	Clearing heat and detoxifying, hemostatic convergence	CRC In Vivo: 300 mg/kg/d, intraperitoneal injection In Vitro: ≤50 μg/mL, in culture medium	PMID:38757413 PMID:26036624
Baicalin	Huangqin	*Scutellariae Radix*	Clearing heat and drying dampness, purging fire and detoxifying	Pan-cancer In Vivo:4 g/kg/d, Oral In Vitro:0.5 mg/mL, in culture medium	PMID:35102626 PMID:36768278 PMID:37337282
A Mixture of Baicalein, Wogonin, and Oroxylin-A	Huangqin	*Scutellariae Radix*			
Homoharringtonine	Xuefei	*Cephalotaxus fortunei*	Clearing away heat and toxic materials	CRC,HCC In Vivo: 1mg/kg, intraperitoneal injection In Vitro: 4μM for 24 h, culture medium	PMID:36126765 PMID:33998239
Fraxetin	Qinpi	*Fraxini Cortex*	Clearing heat and drying dampness	Pan-cancer In Vivo: 25 mg/kg·d) every 3 days for a month, intragastric administration In Vitro: 100μM for 24h, in culture medium	PMID:38501886 PMID:34320467
Sodium new houttuyfonate	Yuxingcao	*Houttuynia cordata*	Clearing away heat and toxic materials	NSCLC In Vivo: 37.5 mg/kg/d, Oral BC 40 mg/kg, intraperitoneal injection	PMID:36696967 PMID:36900408
Dihydroartemisinin	Qinghao	*Artemisia carvifolia*	Clearing away heat and toxic materials	Pan-cancer In Vivo: 45 mg/kg, intraperitoneal injection	PMID:33613116 PMID:34741022
Vinorelbine	Changchunhua	*Catharanthus roseus*	Clearing heat, detoxifying and fighting cancer	NSCLC, 30 mg/m^2, intravenous injection 80 mg/m^2, Oral BC 25 mg/m^2/w, intravenous injection 60 mg/m^2, Oral	PMID:1283851 PMID:10832592

(*Continued*)

Table 1 (Continued).

Compounds Name	Herbs	Latin Name	Traditional use	Application in Tumor, Dosages and Routes of Administration	Reference (PMID)
Berberine	Huanglian	*Coptidis Rhizoma*	Clearing heat and drying dampness, purging fire and detoxifying	Pan-cancer In Vivo: 5 mg/kg, intraperitoneal injection In Vitro: 80 μM, in culture medium	PMID:35889396 PMID:36144625 PMID:31208348
Chlorogenic acid	Jinyinhua	*Lonicerae*	Clearing heat and drying dampness, purging fire and detoxifying	Neuroglioma 40 mg/kg/d, intraperitoneal injection	PMID:36243332 PMID:28045028
Triptonide	Leigongteng	*Tripterygium wilfordii*	Dispel wind and detoxify	Pan-cancer In Vivo: 5mg / kg/d, Oral In Vitro: 0.2 μM, in culture medium	PMID:37062220 PMID:33510281
Honokiol	Houpo	*Houpu Magnolia Officinalis Rehd Et Wils*	Dry dampness eliminating phlegm, under qi removing full	Pan-cancer In Vivo: 100–120 mg/kg, intraperitoneal injection In Vitro: ≥ 50 μM, in culture medium	PMID:30114639 PMID:17487375
CT1-3	Houpo and Xilanhua	*Houpu Magnolia Officinalis Rehd Et Wils/Brassica oleracea L.*		Lung cancer,CRC 20 mg/kg, intraperitoneal injection	PMID:32416457
Ursolic acid	Pipaye	*Eriobotryae Folium*	Removing heat from the lung to relieve cough	Pan-cancer Pancreatic cancer In Vivo: 250 mg/kg/d, Oral In Vitro: 20 μM, in culture medium CRC, 12.5 mg/kg/d, Oral	PMID:36558113 PMID:26909608 PMID:21955093
A Flavonoid Glycoside Compound from Murraya paniculata (L.)	Shilixiang	*Murraya paniculata*	Activating qi to relieve pain, promoting blood circulation and dispersing stasis	Pan-cancer, 100μg/ mL, in culture medium	PMID:28842850
Isoliquiritigenin	Gancao	*Glycyrrhiza uralensis*	Invigorating spleen and replenishing qi	Liver cancer, In Vivo: 2.17 mg/kg, intragastric administration In Vitro: 10 mmol/L, in culture medium Gastric cancer: 4 mg / mL	PMID:30417769 PMID:32425599
18-Glycyrrhetinic Acid	Gancao	*Glycyrrhiza uralensis Fisch*			

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Astragalus polysaccharide	Huangqi	*Astragalus memeranaceus*	Invigorating spleen and replenishing qi	Ascites tumor, In Vivo: 300 mg/kg, intraperitoneal injection Liver cancer, In Vitro: 200 mg/L Ovarian cancer In Vitro: 2 mg/mL Osteosarcoma In Vitro: 10 mg/mL CRC In Vitro: 50 mg/mL NSCLC In Vitro: 30 mg/mL	PMID:38515577 PMID:32159214 PMID:26550164 PMID:30462772
Ganoderma Lucidum Polysaccharide	Lingzhi	*Ganoderma lucidum (Leyss. Ex Fr.) Karst*	Invigorating qi and calming the mind	Pan-cancer In Vivo: 100 mg/kg, intragastric administration	PMID:29141563 PMID:32530032
Osthole	Shechuangzi	*Cnidium monnieri*	Warm kidney and strengthen Yang	Pan-cancer In Vivo: 244 mg/kg, intraperitoneal injection In Vitro: 320 μM, in culture medium	PMID:36160431 PMID:22662241 PMID:29590128
Cinnamaldehyde	Rougui	*Cinnamomum cassia*	Invigorating the kidney and strengthening Yang	Pan-cancer In Vivo: 240 mg/kg, intraperitoneal injection In Vitro: 200 μg/mL, in culture medium	PMID:26890810 PMID:40453666
Puerarin	Gegen	*Puerariae Lobatae Radix*	Expelling wind and clearing heat, raising Yang and raising jin	Lung cancer,GC,CRC,HCC In Vivo: 100 mg/kg, intraperitoneal injection In Vitro: 20 μM, in culture medium	PMID:32021425 PMID:29393465
Acacetin	Taizishen	*Radix Pseudstellariae*	Tonifying qi, invigorating spleen, promoting fluid and moistening lung	Pan-cancer In Vivo: 50 mg/kg, intraperitoneal injection In Vitro: 50 μM, in culture medium	PMID:32866514 PMID:39459239 PMID:28859099
Euphorbia factor L2	Jingdaji	*Radix Euphorbiae Pekinensis*	Purging water to drink, facilitate two stool	Lung cancer,HCC,BC In Vivo: 50 mg/kg, intraperitoneal injection	PMID:28119809 PMID:38063231 PMID:31085375
Cardamonin	Caodoukou	*Alpinia katsumadai*	Change the dampness line qi, warm stop vomiting	Pan-cancer In Vivo: 3 mg/kg/d, intraperitoneal injection	PMID:32224026 PMID:31455352
	Xuanfuhua	*Inula japonica Thunb*	Relieving cough and asthma	BC In Vivo: 10 mg/kg, intraperitoneal injection In Vitro: 10 μM, in culture medium	PMID:26795076 PMID:33065690

(*Continued*)

Table 1 (Continued).

Compounds Name	Herbs	Latin Name	Traditional use	Application in Tumor, Dosages and Routes of Administration	Reference (PMID)
	Tenghaung	*Garcinia hanburyi*	Dispelling rot to heal sores and attack poison	CRC	PMID:37292335
	Diyu	*Radix Sanguisorbae*	Cooling blood to stop bleeding,detoxification to heal sores	CRC In Vitro: 0.8μg/mL, in culture medium	PMID:34659228 PMID:37292335
	Qulian	*Hemsleya amabilis Diels*	Clearing heat and detoxifying, diuresis and analgesia	Renal cell carcinoma In Vivo: 300 mg/kg, intragastric administration In Vitro: 20μg/mL, in culture medium	PMID:37557938
	Chonglou	*Paris polyphyllaSmith var.chinensis (Franch.) Hara*	Clearing heat and detoxifying, reducing swelling and relieving pain	Pan-cancer In Vivo: 350 mg/kg, intragastric administration In Vitro: 20 and 60μg/mL, in culture medium	PMID:31870841 PMID:26147856
	Yougan	*Pomelo*	Anticancer and anti-ulcer	CRC,GC In Vivo: 2mg/kg/d, intraperitoneal injection In Vitro: 0.71–2.85 mM, in culture medium	PMID:37367061 PMID:34490484 PMID:29928387 PMID:35884991
	Quanxie	*Buthus martensii Karsch*	Used for calming wind and relieving spasmodic, attacking poison and dispersing knot, clearing collaterals and relieving pain	Bone cancer,Lymphoma cell line,BC,Lung cancer In Vivo: 108 mg/200 g/d, intragastric administration In Vitro: 60μM, in culture medium	PMID: 32052691 PMID:19373662 PMID:30740360 PMID:38850481

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Table 2 TCM Understanding of Formulae

Name	Composition	Traditional Use	Application in Tumor	Reference (PMID)
BuFei decoction (BFD)	**Radix Codonopsis** (dried root of *Codonopsis pilosula*(Franch.) Nannf.,Dangshen, in *Campanulaceae*); **Radix Astragali** (dried root of *Astragalus membranaceus* (fisch.) Bunge., Huangqi, in *Leguminosae*); **Fructus Schisandrae** (dried fruit of *Schisandra chinensis* (Turcz.) Bail., Wuweizi, in *Schisandraceae*; **Radix Rehmanniae** (dried root of *Rehmannia glutinosa* (Gaertn.) DC., Dihuang, in *Scrophulariaceae*; **Aster Root** (dried root tuber of *Aster tataricus* L.f., Ziyuan, in *Compositae*; **Cortex Mori** (dried root bark of *Morus alba* L., Sangbaipi, in *Moraceae*)	Tonifying lung qi, reducing the reverse cough	NSCLC	PMID: 36070661
Babao Dan (BBD)	**Calculus Bovis**(Liverstone or gallstone of *Bos taurus domesticus Gmelin*, Niuhuang,in *Bovid*); **Snake Bile**(*Python molurus bivittatusSchlegel*,Shedan, in *Colubridae*); **Cornu Saigae Tataricae** (horn of *Saigae tataricae cornu*,Lingyangjiao,in *Compositae*); **Pernulo**(powder of *Pteria martensii* (Dunker.),Zhenzhu, in *Pteriidae*); **Radix Notoginseng**(dried root of *Panaxnotoginseng*(Burk.) F. H.Chen,Sanqi,in *Araliaceae*); **Moschus moschiferus L** (dry secretion of mature male sachets of *MoschusberezovskiiFlerov*, M. *sifanicusprzewalski*, or M. *oschiferusLinnaeus*,Shexiang,in *Cervidae*)	Clearing heat and detoxifying, promoting blood circulation and removing blood stasis, removing saprophyte and producing new, removing cold and relieving pain	PC,GC,HCC	PMID: 31456462 PMID: 33330063 PMID: 37251918
Fuzheng Xiaojijinzhan decoction (FZXJJZF)	**Astragalus memeranaceus**(dried root of *Astragalus membranaceus* (Fisch.) Bunge.,Huangqi,in *Leguminosae*); **Atractylodes macrocephala Koidz** (dried root of *Atractylodes macrocephala Koidz*,Baizhu,in *Compositae*); **Ganoderma lucidum**(fruiting body of *Ganoderma lucidum*,Lingzhi, in *Ganodermataceae*); **Coix lacryma-jobi L**(seeds of *Coix lacryma-jobi var. stenocarpa* Oliv., Yiyiren,in *Gramineae*);**Hedyotis diffusa Willd**(grass of *Oldenlandia diffusa* (Willd.) Roxb., Baihuasheshecao,in *Rubiaceae*);**Buthus martensi Karsch**(insect of *Buthus martensi* Karsch, Quanxie,in *Buthidae*);**Prunella vulgaris L**(fruit ear of *Prunella vulgaris subsp. lanceolata* (W.P.C. Barton) Piper & Beattie,Xiakucao,in *Labiatae*);**Curcuma wenyujin Y.H.Chen et C.Ling** (rhizome of *Curcuma zedoaria* (Christm.) Roscoe,Ezhu,in *Zingiberaceae*)	Invigorating qi and invigorating spleen, clearing heat and detoxifying	CRC	PMID: 34952191
Ruyong formula(RYF)	**Radix Codonopsis** (dried root of *Codonopsis pilosula* (Franch.) Nannf.,Dangshen,in *Campanulacea*);**Radix Astragali** (dried root of *Astragalus membranaceus* (fisch.) Bunge.,Huangqi, in *Leguminosae*);**Radix Astragali Sinensis**(dried root of *Angelica Sinensis* (Oliv.) Diels,Danggui, in *Umbelliferae*);**Radix Bupleurum** (dried root of *Bupleurum chinense* DC.,Chaihu,in *Umbelliferae*);**Ligusticum sinense "Chuanxiong"**(rhizome of *Ligusticum chuanxiong* Hort., Chuanxiong,in *Umbelliferae*);**Radix Paeoniae Alba**(dried root of *Paeonia lactiflora* Pall., ShengBaiShao,in *Ranunculaceae*);**Forsythia suspensa (Thunb.) Vahl**(fruit of *Forsythia suspensa* (Thunb.) Vahl,Lianqiao,in *Oleaceae*);**Glycyrrhiza uralensis Fisch** (rhizome of *Glycyrrhiza uralensis* Fisch.,Gancao,in *Leguminosae*);**Trichosanthes kirilowii Maxim** (fruit of *Trichosanthes kirilowii* Maxim.,Gualou,in *Cucurbitaceae*);**Cortex fraxini** (fruit of *Citrus reticulata* Blanco,Qingpi, in *Oleaceae*)	Clearing heat and detoxifying, promoting blood circulation and removing stasis	BC	PMID: 37717843

(*Continued*)

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Table 2 (Continued).

Name	Composition	Traditional Use	Application in Tumor	Reference (PMID)
Biejiajian Pill(BJJP)	**Trionycis Carapax** (carapace of *Trionyx sinensis* Wiegmann,Biejia,in *Trionychidae*);**Colla corii asini**(skin of *Equusasinus*L.,Ejiao,in *Equidae*);**Vespae Nidus**(nest of *Polistes mandarinus* Saussure, Fengchao,in *Vespidae*);**Armadillidium**(dried body of *Armadillidium vulgare* (Latrielle), Shufu,in *Oniscidae*);**Coleoptera**(dried body of *Eupolyphaga seu Steleophaga*,Tubie,in *Coleoptera*); **Geotrupidae**(body of *Catharsius molossus* (Linnaeus),Qianglang,in *Scarabaeidae*);**Saltpeter** (mineral traditional Chinese medicine);**Radix Bupleurum** (dried root of *Bupleurum chinense* DC.,Chaihu,in *Umbelliferae*);**Radix Scutellariae**(*Scutellaria baicalensis Georgi*,Huangqin,in *Labiatae*);**Pinellia**(dried root of *Pinellia ternata* (Thunb.) Ten. ex Breitenb.,Banxia,in *Araceae*); **Radix Codonopsis** (dried root of *Codonopsis pilosula*(Franch.) Nannf.,Dangshen, in *Campanulaceae*);**Zingiber officinale Roscoe**(dried root of *Zingiber officinale* Roscoe, Shengjiang,in *Zingiberaceae*);**Magnolia officinalis**(dried bark of *Houpu Magnolia Officinalis* Rehd Et Wils,Houpo,in *magnoliaceae*);**Ramulus Cinnamomi**(dried shoots of *Cinnamomum cassia Presl*.,Guizhi,in *Lauraceae*);**Radix Paeoniae Alba**(dried root of *Paeonia sterniana* H. R. Fletcher, Baishao,in *Ranunculaceae*); **Rhizoma belamcandae**(dried root of *Belamcanda chinensis* (L.) DC.,Shegan,in *Iridaceae*);**Prunus persica**(Kernel of *Prunus persica*(L.)Batsch,Taoren,in *Rosaceae*); **Cortex moutan**(dried root skin of *Paeonia suffruticosa* Andr, Mudanpi,in *Ranunculaceae*); **Rheum officinale**(dried root of *Rheum officinale Baill*.,Dahuang,in *Polygonaceae*);**Campsis grandiflora**(flower of *Campsis grandiflora*(Thunberg) Loisel,Linxiao,in *Bignoniaceae*);**Semen Lepidii** (dried seeds of *Semen Lepidii Semen* Descurainiae,Tinglizi,in *Cruciferae*);**Pyrrosia**(leaf of *Pyrrosia lingua*(Thunb.)Farw.,Shiwei,in *polypodiaceae*);**Dianthus superbus**(*Dianthus superbus* L., Qumai,in *Caryophyllaceae*)	Eliminating ruffian and accumulation, promoting blood circulation and removing stasis, soothing liver and relieving depression	HCC	PMID: 37222832 PMID: 34899325
Jiedu Sangen Decoction (JSD)	**Actinidia argute Siebold & Zucc** (dried root of *Actinidia argute*(Sieb.et Zucc.)Planch.Ex Miq., Ruanzao mihoutao,in *actinidiaceae*); **Adina fauriei H.Lév**. (dried root of *Nauclea rubella* (Hance) Nakai,Maidong,in *Rubiaceae*); **Reynoutria japonica Houtt** (dried root of *Rhizoma Polygoni* Cuspidati,Huzhang,in *Polygonaceae*)	Sour and astringent solid intestine, clear damp heat	CRC	PMID: 36606189 PMID: 33641785
Ruyiping formula (RYP)	**Iphigenia indica Kunth** (dried root of *Iphigenia indica* Kunth,Shancigu,in *Colchicaceae*);**Vespae Nidus**(nest of Polistes mandarinus Saussure,Fengchao,in *Vespidae*);**Curcuma wenyujin Y.H. Chen et C.Ling**(rhizome of *Curcuma zedoaria* (Christm.) Roscoe,Ezhu,in *Zingiberaceae*);**Coix lacryma-jobi L**(seeds of *Coix lacryma-jobi var. stenocarpa* Oliv.,Yiyiren,in *Gramineae*);**Akebiae Fructus** (seeds of *Fructus Alebiae*,Bayuezha,in *Lardizabalaceae*)	Remove toxin, dissipate nodule and eliminate swell and stagnation	BC	PMID: 30901274 PMID: 31517546
Banxia Xiexin decoction (BXXXD)	**Pinellia**(dried root of *Pinellia ternata* (Thunb.) Ten. ex Breitenb.,Banxia,in *Araceae*);**Makino** (whole grass with roots of *Viola yedoensis* Makino,Zihuadiding,in *Violaceae*);**Radix Scutellariae** (*Scutellaria baicalensis* Georgi,Huangqin,in *Labiatae*);**Panax L**.(dried root of *Panax ginseng* C.A. Mey.,Renshen,in *Araliaceae*);**Ziziphus jujuba Mill**(dried fruits of *Ziziphus jujuba* Mill,Dazao,in *Rhamnaceae*);**Zingiber officinale Roscoe**(dried root of *Zingiber officinale* Roscoe,Shengjiang,in *Zingiberaceae*)	Harmonizing liver and spleen, cold and heat leveling, eliminating ruffiness and dispersing knot	GC,CRC	PMID: 37657053 PMID: 34278452
Xianlinglianxiafang (XLLXF)	**Radix Codonopsis** (dried root of *Codonopsis pilosula*(Franch.) Nannf.,Dangshen, in *Campanulaceae*);**Poria cocos Wolf**.(dried sclerotium of *Wolfiporia cocos* (F.A. Wolf) Ryvarden & Gilb.,Fuling,in *Liliaceae*);**Epimedium brevicornu Maxim**.(stem and leaf of *Epimedium brevicornu* Maxim.,Yinyanghuo,in *Berberidaceae*);**Prunella vulgaris L**(fruit ear of *Prunella vulgaris subsp. lanceolata* (W.P.C.Barton) Piper & Beattie,Xiakucao,in *Labiatae*);**Curcuma wenyujin Y.H. Chen et C.Ling**(rhizome of *Curcuma zedoaria* (Christm.) Roscoe,Ezhu,in *Zingiberaceae*);**Radix Scutellariae**(*Scutellaria baicalensis* Georgi,Huangqin,in *Labiatae*)	Detoxifying and eliminating accumulation	TNBC	PMID: 37478577

Fuzheng KangAi decoction (FZKAD)	**Atractylodes macrocephala Koidz** (dried root of *Atractylodes macrocephala* Koidz,Baizhu,in *Compositae*);**Pseudostellaria heterophylla (Miq.) Pax** (dried root of *Pseudostellaria heterophylla* (Miq.)Pax ex Pax et Hoffm.,Taizishen,in *Caryophyllaceae*);**Radix Astragali** (dried root of *Astragalus membranaceus* (fisch.) Bunge.,Huangqi, in *Leguminosae*);**Hedyotis diffusa Willd**(grass of *Oldenlandia diffusa* (Willd.) Roxb., Baihuasheshecao,in *Rubiaceae*);**Solanum nigrum L**.(dried herba of *Solanum nigrum* L.,Longkui,in *Solanaceae*);**Iphigenia indica Kunth** (dried root of *Iphigenia indica* Kunth,Shancigu,in *Colchicaceae*);**Salviae Chinensia**(dried herba of *Salvia japonica* Thunb,Shuweicao,in *Lamiaceae*);**Coix lacryma-jobi L**(seeds of *Coix lacryma-jobi var. stenocarpa* Oliv.,Yiyiren,in *Gramineae*);**Akebia quinata**(dried roots and stems of *Akebia quinata* (Thunb.) Decne (Bayuezha),Wuyemutong,in *Lardizabalaae*);**Rubus parvifolius L**.(dried leaf and stems of *Rubus parviflolius* L. (Shepaole),Maomei,in *Rosaceae*);**Curcuma wenyujin Y.H. Chen et C.Ling**(rhizome of *Curcuma zedoaria* (Christm.) Roscoe,Ezhu,in *Zingiberaceae*); **Glycyrrhiza uralensis Fisch** (rhizome of *Glycyrrhiza uralensis* Fisch.,Gancao,in *Leguminosae*)	Fuzheng dispels evil, detoxification detumescence	NSCLC	PMID: 32489321
Jinfukang (JFK)	**Radix Astragali** (dried root of *Astragalus membranaceus* (fisch.) Bunge.,Huangqi, in *Leguminosae*);**Glehniae Radix**(dried root of *Glehnia littoralis* F. Schmidt ex Miq.,Beishashen,in *Apiaceae*);**Adina fauriei H.Lév**. (dried root of *Nauclea rubella* (Hance) Nakai,Maidong,in *Rubiaceae*);**Fructus Ligustri Lucidi**(dried fruits of *Ligustrum lucidum* Ait,Nvzhenzi,in *Oleaceae*); **Cornus officinalis** (dried fruits of *Cornus officinalis* Sieb. et Zucc.,Shanzhuyu,in *Cornaceae*); **Gynostemma pentaphyllum** (whole herb of *Gynostemma pentaphyllum*(Thunb.) Makino var. pentaphyllum,Jiaogulan,in *Cucurbitaceae*);**Epimedium brevicornu Maxim**.(stem and leaf of *Epimedium brevicornu* Maxim.,Yinyanghuo,in *Berberidaceae*);**Trigonella foenum-graecum L**. (dried seeds of *Trigonella foenum-graecum* L.,Huluba,in *Leguminosae*);**Selaginella doederleinii Hieron**.(whole herb of *Selaginella doederleinii* Hieron.,Shishangbai,in *Selaginellaceae*);**Salviae Chinensia**(dried herba of *Salvia japonica* Thunb,Shuweicao,in *Lamiaceae*);**Paris polyphylla** (rootstock of *Paris polyphyllaSmith var.chinensis* (Franch.) Hara,Chonglou,in *Melanthiaceae*); **Asparagus cochinchinensis**(dried root of *Asparagus cochinchinensis* (Lour.) Merr.,Tiandong,in *Liliaceae*)	Invigorating qi and nourishing Yin, clearing heat and detoxifying	NSCLC	PMID: 33933571

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Table 3 Potential Mechanism of TCM Targeting EMT Mediating Anoikis

TCM	Name	Targets	Pathway	Application in tumor	Animal model/Cell line	Reference (PMID)
Compounds	Honokiol (HNK)	Snail,Slug,E-cadherin, and Vimentin		Breast cancer	Female BALB/c nude mice (6–8 weeks old) The human mammary epithelial tumor cell lines MCF7 and MDA-MB-231 and mouse mammary tumor cell line 4T1	PMID: 31235819
	CT1-3	E-cadherin/Snail axis		Lung cancer/ Colorectal	H460 and LOVO cell lines	PMID: 32416457
	Rosthorin A	Slug, Twist, E-cadherin, N-cadherin, Vimentin, and β-catenin		NSCLC	A549, H1299, and H1975 cells	PMID: 33065690
	Isoliquiritigenin (ISL)	ZEB1,ZEB2,Twist1,E-cadherin,Vimentin and N-cadherin		Ovarian cancer	Tumor-bearing mice/SKOV3 and OVCAR5 cells	PMID: 31623144
	Triptonide	Twist1,VE-cadherin, VEGFR2, and N-cadherin	NF-κB signaling pathway	TNBCs	NOD-SCID female mice (18–22 g) /TNBC cell lines MDA-MB-231, MDA-MB-468, and BT-549	PMID: 34922602
	Astragalus polysaccharide	E-cadherin,β-catenin, Snail, vimentin, c-Myc and Cyclin D1	Wnt/β-catenin signaling pathway	Breast cancer	MCF-7 and MDA-MB-231 cells	PMID: 32319619
	Gallic acid	E-cadherin,N-cadherin and Vimentin,Cyclin D1, β-catenin	Wnt/β-catenin Signaling Pathway	Gastric precancerous lesions	40 BABL/C mice (specific pathogen free grade, 4-weeks-old, 18–20 g, half male and half male), N-Nitroso-N-methylurea (MNU)-induced GPL mice model/Gastric mucosal epithelial cells GES-1 and MC cell	PMID: 36328204
	Euphorbia factor L2	Vimentin,N-cadherin,p-AKT,p-STAT3,E-cadherin	AKT and STAT3 signaling	Hepatocellular carcinoma	Thirty Male BALB/c athymic nude mice (5–6 weeks old, 15–18 g)/Human hepatocellular carcinoma cells HEPG2 and SMMC-7721	PMID: 31085375
	Naringin	Cyclin D1,Bcl-2,Caspase-3,P21,Bax and Cleaved Caspase-3,Vimentin, ZEB1 and P-AKT,E-cadherin	PI3K/AKT Signaling Pathway	Gastric cancer	Adult BALB/C nude mice (female, age 35 to 40 days, weight 18g to 22g) human gastric cancer cell lines, MGC803 and MKN45	PMID: 36112793
	Homoharringtonine	Slug,E-cadherin,N-cadherin and Vimentin,Bcl-2, Bax, Snail,Twist	PI3K/AKT/GSK3β/Slug signaling pathway	Hepatocellular carcinoma	BALB/c nude mice (4–5 weeks old)/Human liver cells (L-02) and HCC cell lines (HCCLM3, HepG2, and Huh7)	PMID: 33998239
	18-Glycyrrhetinic Acid	E-cadherin,Occludin and Fibronectin,Snail	SHP1&SHP2/STAT3/Snail pathway	Hepatocellular carcinoma	Two hepatoma cell lines (Bel-7402 and LM3)	PMID: 34963428
	A Flavonoid Glycoside Compound from Murraya paniculata (L.)	Integrin β1,EGFR,COX-2,MMP-2,MMP-9,N-cadherin, vimentin and E-cadherin	STAT3/NF-κB/COX-2 and EGFR Signaling Pathways	Lung adenocarcinoma	Human non-small cell lung cancer A549 and PC9 cells	PMID: 28842850
	Acacetin	TGF-β1,E-cadherin, N-cadherin, Vimentin, MMP-9, MMP-2 and Snail	PI3K/Akt/Snail pathway	Gastric cancer	Male BALB/c nude mice (21–25 g weight; 4–6 weeks old) The human GC cell lines MKN45 and MGC803	PMID: 35000605
	Fraxetin	N-cadherin,snail,vimentin,TLR4,phosphorylated(P)-STAT3,cyclin D1,C-myc and E-cadherin	TLR4/STAT3 signaling pathway	Ovarian cancer	SKOV3 and SW626 cells	PMID: 36346016
	Ganoderma Lucidum Polysaccharide	Bax,Cleaved Caspases 3 and 9,Bcl-2,E-cadherin, N-cadherin,Vimentin and Slug	JAK/STAT5 Signaling Pathway	Cervical cancer	Human cervical immortalized squamous cells Ect1/E6E7, humancervical carcinoma cells C-33A, HeLa	PMID: 31995806

	Puerarin	miR-21,PTEN/AKT,E-cadherin,N-cadherin,Vimentin, Slug,Snail	miR-21-mediated PTEN/AKT signaling	Hepatocellular carcinoma	Male BALB/c nu/nu mice (4–5 weeks old) /Bel-7402, Huh7, and L02	PMID: 32294699
	Sodium new houttuyfonate	linc00668,Slug,E-cadherin,N-cadherin,Vimentin,	linc00668/miR-147a/Slug axis	NSCLC	BALA/c nude mice/NCI-H1299, A549, NCI-H460 and 293 T cells,SK-MES-1, SPC-A1 and HBE cells	PMID: 30971296
	Dihydroartemisinin	E-cadhein,Vimentin,Akt,p-Akt,and Snail	PI3K/AKT signaling pathway	Gastric cancer	Gastric cancer cell line SGC7901	PMID: 31187708
	Vinorelbine	E-cadherin,N-cadherin,vimentin,Snail,MMP-2 and MMP-9		Lung cancer, Liver cancer and Colon cancer	Human lung adenocarcinoma cell line NCI–H1975 (H1975),Human hepatoma cell line HepG2,Human colon cancer cells line HCT116	PMID: 32473523
	Cardamonin	ADRB2,MMP-2,MMP-9,N-cadherin and E-cadherin		Lung metastasis of colorectal cancer	Six-week-old female BALB/c nude mice Human CRC cell lines HT29 (HTB-38) and HCT116 (CCL-247) as well as human normal colorectal fibroblasts CCD-18Co (CRL-1459)	PMID: 35645356
	Osthole	ITGα3 and ITGβ5	FAK/Src/Rac1 pathway	Breast cancer	Zebrafish Human breast cancer cell lines MCF-7, MDA-MB-231, T-47D, SK-Br-3, MDA-MB-231BO,lentivirus packaging cells HEK293T,Human normal mammary epithelial MCF-10A cell lines	PMID: 34426644
	Berberine	TGF-β,TβRI, TβRII, Smad2/p-Smad2 and Smad3/ p-Smad3,E-cadherin,Vimentin,α-SMA,ZEB1 and Snail, Bax, Bcl-2.	The Smad-dependent and Smad-independen t TGF-β signalling pathways	Colonic epithelial	Human normal colonic epithelial cell line HCoEpiC,human colonic myofibroblast line CCD-18Co cells	PMID: 31399854
	Chlorogenic acid	p-IκBα and N-cadherin,PD-L1,cleaved caspase-3	NF-κB and EMT signaling pathways increasing the proportion of CD4 and CD8 T cells in spleens	Breast cancer	Twenty-seven female BALB/c mice (age, 6–8 weeks; weight, 18–20 g) human breast cancer cell lines MDA-MB-231 and MDA-MB-453, human mammary epithelial cells MCF-10A and the murine breast cancer cell line 4T1	PMID: 33416150
	Cinnamaldehyde	Bax,cleaved-PARP,E-cadherin,N-cadherin,Vimentin, MMP-9,VEGF and β-catenin	Wnt/β-catenin pathway	NSCLC	BALB/c/nu/nu nude mice (6–8 week old) Human NSCLC cell lines A549, YTMLC-90 and NCI-H1299	PMID: 28093328
	Ursolic acid	TGF-β1,phosphorylated (p)-Smad2/3,p-focal adhesion kinase and ZEB1	TGF-β1/ZEB1/miR-200c signaling pathway	Colorectal cancer	Human CRC RKO cells	PMID: 33549076
	Ursolic acid	Bcl-2,Bax,caspase-3,-8and-9,N-cadherin and E-cadherin	Arrested the cell cycle at the G0/ G1 phase	Colorectal cancer		
	A Mixture of Baicalein, Wogonin, and Oroxylin-A	Twist1,E-cadherin,N-cadherin,p-Akt,Vimentin	PI3K/AKT-TWIST1-Glycolysis Pathway	NSCLC	The A549 cells	PMID: 35222014
	Ethyl acetate extract of Caesalpinia sappan L.	MMP,Bax and Bcl-2,caspase-9 and −3,Mff and Fis1	ROS-mediated apoptosis and differentiation	Acute myeloid leukemia	Four-week-old nonobese diabetic/severe combined immunodeficiency (NOD/ SCID) mice HL-60 and Kasumi-1 cells	PMID: 32045840
	A Novel Aniline Derivative from Peganum harmala L.	mTOR,ROS,Bax,caspase-3,p-cyclinD1 and p-Erk1/2, CD133	PI3K/AKT/mTOR and EMT pathways	NSCLC	Human non-small cell lung cancer A549 and PC9 cells	PMID: 37628807

(*Continued*)

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Table 3 (Continued).

TCM	Name	Targets	Pathway	Application in tumor	Animal model/Cell line	Reference (PMID)
Herbs	*Inula japonica Thunb*	ZEB1,MMP-9,and CD44		TNBCs	Mouse model of experimental lung metastasis with 4T1 cells/Human breast carcinoma cell lines MDA-MB-231 and MDA-MB-435 and human breast epithelial cell line MCF10A	PMID: 35839735
	Gamboge	β-catenin,MMP-7,Cyclin D1,and E-cadherin	Wnt/β-catenin Signaling Pathway	Colon cancer	BALB/C male nude mice, Orthotopic mouse model of colon cancer (4–6 weeks old) /The human colon cancer cell line SW480-GFP	PMID: 29599307
	Sanguisorba	Bax,cleaved-caspase3,cleaved-PARP,Bcl-2,N-cadherin, Vimentin,Snail,E-cadherin	Wnt/β-catenin Signaling Pathway	5-fluorouracil-sensitive and-resistant colorectal cancer	Eighteen male BALB/C nude mice/RKO-P and HCT15-P cells represent 5-FU-senstive cells,RKO-R and HCT15-R cells represent 5-FU-resistant cells	PMID: 34785413
	Root extract of *Hemsleya amabilis Diels*	Bax,Bcl-2,PARP,cleared-PARP,Caspase-9,Caspase-8, Caspase-3,Survivin,Cyclin-B1,CDK1,N-cadherin, Snail,Slug,E-cadherin and MMP-9	PI3K/AKT signaling pathway	Renal cell carcinoma	Twenty-one female BALB/c nude mice (5–6 weeks) the human renal cell carcinoma cell line OS-RC-2 and the human renal cell adenocarcinoma cell line ACHN,the human clear renal cell carcinoma cell line RCC4	PMID: 37557938
	Scorpion	LC3*II* and Beclin1,P62,GDPD4-2	GDPD4-2/PI3K/AKT/mTOR Pathway	Prostate Cancer	110 male BABL/c nude mice (4–6 weeks) Human normal prostate epithelial cells RWPE-1 cells (iCell-h286, iCell) and human prostate cancer cell line LNCaP (CL-0143, Procell)	PMID: 35847007
	Root extract of *Hemsleya amabilis Diels*	Bax,Bcl-2,PARP,cleared-PARP,Caspase-9,Caspase-8, Caspase-3,Survivin,Cyclin-B1,CDK1,N-cadherin, Snail,Slug,E-cadherin and MMP-9	G2/M phase arrest via PI3K/AKT signaling pathway	Renal cell carcinoma	Twenty-one female BALB/c nude mice (5–6 weeks) Human renal cell carcinoma cell line OS-RC-2,human renal cell adenocarcinoma cell line ACHN,human clear renal cell carcinoma cell line RCC4	PMID: 37557938
	Paris polyphylla ethanol extract	Cadherin-1 (CDH1),cadherin-2 (CDH2),Snail family transcriptional repressor 2 (SNAI2), and Twist family bHLH transcription factor 1 (TWIST1)	Regulated the levels of cell cycle-associated proteins	Bladder cancer	Six-week-old male BALB/c nude mice J82 BC-derived cell line	PMID: 35117211
Formulae	Bu-Fei decoction (BFD)	E-cadherin,N-cadherin,Vimentin, Fibronection	TGF-β1-smad Signaling Pathway	NSCLC	Female BALB/C nude mice with body weight of 18–20 g The human NSCLC A549 cell line	PMID: 28412214
	Babao Dan (BBD)	p-Smad2/3,N-cadherin,E-cadherin, Vimentin, ZEB1, ZEB2, Twist1, MMP2, MMP9, TGF-β1	TGF-β-smad Signaling Pathway	Gastric cancer	The human GC cell lines AGS and MGC80-3	PMID: 32529872
	Fuzheng Xiaojijinzhan (FZXJJZF) decoction	VDR,E-cadherin,TGF-β,Snail1	VDR/TGF-β/Snail1 signaling pathways	Colorectal cancer liver metastasis	Nude mice HCT-116 cells	PMID: 34952191
	Ruyong formula (RYF)	Snail 1,ZEB 1,Smad,p-STAT3, p-JAK2, E-cadherin, and p-PI3K p55,TSLP and Vimentin	JAK2/STAT3/PI3K pathway	Breast cancer	BALB/c mice (4–6 w, Female)mouse breast cancer cell line (4T1),Thymic epithelial cells (TECs)	PMID: 37717843
	Biejiajian Pill (BJJP)	N-cadherin,p-Akt (Ser473),p-GSK-3β (Ser9),Snail, Vimentin and E-cadherin,Cyclin D1,MMP-9 and VEGFA	Akt/GSK-3β/Snail Signaling Pathway	Hepatocellular carcinoma	Four to five weeks old female BALB/c nude mice (15–16 g) The MHCC-97H, as well as SMMC-7721 human HCC cell lines	PMID: 33762939
	Jiedu Sangen Decoction (JSD)	Cyclin D1,survivin,Bcl-2,N-cadherin,Snail, Bax and E-cadherin,Vimentin, p-AKT1, AKT1, p- GSK-3β, Slug, and Twist	AKT/GSK-3β signaling pathway	Colon cancer	nude mice SW480, SW620 and HCT-8 cells	PMID: 31772677

	Ruyiping formula (RYP)	Slug,E-Cadherin, N-Cadherin and miR-134	microRNA-134-Slug	Breast cancer	BALB/c mice/Human breast carcinoma cell line MDA-MB-231 and mouse mammary carcinoma cell line 4 T1	PMID: 34225726
	Banxia Xiexin decoction (BXXXD)	lncRNA TUC338,E-cadherin,N-cadherin,Vimentin	PI3K/AKT signaling pathway	Gastric cancer	The human gastric cancer cell lines AGS and GES-1	PMID: 37964840
	Xian-ling-lian-xia-fang (XLLXF)	VEGFA,MMP2,MMP9,Vimentin,E-cadherin,Twist1, E-cadherin and tissue inhibitors of metalloproteinase (TIMP)-1,TIMP-3	VEGF/MMPs pathway	Breast cancer	Seven-week-old female nude BALB/c mice (18–20 g) Human TNBC cell line MDA-MB-231	PMID: 35379271
	Fuzheng Kang-Ai decoction (FZKAD)	N-cadherin and Vimentin	STAT3/MMP9 pathway	Lung cancer	Cells Human A549 NSCLC cells,PC9 and H1650 cells	PMID: 28677797
	Jinfukang (JFK)	Fibronectin1,Integrin β1,p-Src,p-MEK,p-ERK1/2, MMP2 and MMP9	Integrin/Src pathway	Lung cancer	Human circulating lung cancer cell line CTC-TJH-01,H1975 cells	PMID: 33068649

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EMT and enhancing resistance to anoikis. For example, honokiol, a major bioactive compound from *Magnolia officinalis*, CT1-3, a novel hybrid derived from *Magnolia officinalis* and *Brassica oleracea L.*, and Rosthorin A, extracted from *Isodon rosthornii*, have all been reported to downregulate Snail/Slug and promote E-cadherin expression, thereby inhibiting EMT.[79–81] Both *Inulae Flos* and *Magnolia officinalis* are qi-regulating drugs. Unlike Honokiol, which targets Snail, *Inula japonica* Thunb specifically binds to ZEB1 in triple Negative Breast Cancer (TNBC) and induces its ubiquitination to suppress cell invasion and metastasis.[82] In ovarian cancer, Isoliquiritigenin (extracted from *Glycyrrhiza uralensis* Fisch) similarly inhibits metastasis by targeting ZEB1. Additionally, triptonide (from *Tripterygium wilfordii*) has been shown to induce the lysosome-mediated degradation of Twist1, subsequently reducing Notch1 expression and NF-κB phosphorylation.[83]

Most TCM agents exert their regulatory effects on EMT and anoikis through upstream signaling pathways rather than direct interaction with TFs. The Wnt/β-catenin, TGF-β/Smad, and PI3K/AKT pathways are most frequently implicated. Various compounds—such as Astragalus polysaccharides (*Astragalus membranaceus*), extracts from *Garcinia hanburyi*, gallic acid (*Rhus chinensis*), Euphorbia factor L2 (*Euphorbia pekinensis*), and *Radix Sanguisorbae*—have been shown to inhibit EMT via modulation of the Wnt/β-catenin pathway.[84–89] *Radix Sanguisorbae* has shown significant efficacy in 5-fluorouracil-sensitive and resistant CRC.[88] Several TCM formulas targeting the TGF-β/Smad pathway have also been identified, including BFD, BBD, FZXJJZF, and RYF.[90–93] In addition, compounds such as pomelo, *Hemsleya amabilis*, and acacetin (from Radix Pseudostellariae) inhibit tumor invasion and metastasis via regulation of the PI3K/AKT signaling pathway.[94–96] Notably, glycogen synthase kinase-3 (GSK-3) acts as a downstream effector of this pathway, mediating the expression of EMT-related TFs. The formulas BJJP and JSD have been shown to suppress liver and colon cancer metastasis via the AKT/GSK-3β/Snail axis,[97,98] while Homoharringtonine (extracted from *Cephalotaxus hainanensis*) targets the PI3K/AKT/GSK-3β/Slug pathway to inhibit liver cancer progression.[99] The JAK/STAT signaling pathway also plays a central role. STATs are activated through JAK-mediated phosphorylation and translocate to the nucleus to regulate target gene transcription.[100] TCM compounds such as 18-β-glycyrrhetinic acid (*Glycyrrhiza uralensis*), a flavonoid glycoside from *Murraya paniculata*, and fraxetin (from Fraxini Cortex) have all been reported to inhibit STAT3 activity,[101,102] while Ganoderma Lucidum Polysaccharide (extracted from *Ganoderma lucidum*) suppresses EMT in cervical cancer via the JAK/STAT5 pathway.[103]

Recent studies have also highlighted the role of TCM in regulating non-coding RNA networks. For example, puerarin (from *Pueraria lobata*) inhibits EMT and suppresses hepatocellular carcinoma (HCC) metastasis by modulating the miR-21/PTEN/AKT pathway.[104] In breast cancer (BC), the TCM formula RYP has been shown to suppress tumor metastasis via the miR-134/Slug axis.[105] Sodium new houttuyfonate (extracted from *Houttuynia cordata* Thunb) targets the linc00668/miR-147a/Slug axis, while BXXXD targets lncRNA TUC338 to mediate EMT.[106,107]

In addition, some TCMs directly alter ECM components, such as upregulating the epithelial marker E-cadherin and downregulating the mesenchymal marker N-cadherin, thereby mediating EMT. Dihydroartemisinin, a derivative of *Artemisia carvifolia*, has been found to effectively inhibit gastric carcinoma (GC) proliferation. Furthermore, increasing drug concentrations significantly enhances E-cadherin expression while inhibiting the protein expression of the mesenchymal marker Vimentin.[108] Scorpion (*Buthus martensii* Karsch), the dried whole scorpion of the Buthidae family, is commonly used in TCM to treat internal and external wind-related conditions, such as infantile convulsions, facial paralysis due to stroke, hemiplegia, tetanus, and rheumatism. Its compatibility with *Astragalus* in treating tumors has also been validated by modern molecular biomedical research.[109] Studies have found that Scorpion promotes E-cadherin and inhibits N-cadherin to mediate EMT.[110] Alkaloids extracted from *Catharanthus roseus* have long been used in oncology; notably, vinorelbine modulates the expression of E-cadherin, N-cadherin, vimentin, Snail, and matrix metalloproteinases MMP-2 and MMP-9, thereby suppressing cancer cell invasion and metastasis.[111] Vinorelbine (extracted from *Catharanthus roseus*) regulates E-cadherin, N-cadherin, Vimentin, and Snail, MMP-2, and MMP-9 to inhibit cancer cell metastasis. Integrins and MMPs play important roles in maintaining ECM structural stability.[112] It has been reported that Cardamonin (extracted from *Alpinia katsumadai*) effectively reduces MMP-2 and MMP-9 expression in tumor cells, thereby increasing ECM adhesion effects.[113] Similarly, TCM formulas such as XLLXF and FZKAD have similar effects.[114] Other agents, including JFK and osthole (from *Cnidium monnieri*), regulate ECM dynamics through the integrin/Src pathway and ITGα3/ITGβ5 signaling, respectively.[115]

Regulation of Apoptotic Genes

Some TCMs exert anti-tumor effects primarily by regulating apoptosis-related genes downstream of EMT-associated signaling pathways. For instance, berberine (extracted from Coptidis Rhizoma) has been shown to inhibit EMT through the TGF-β pathway, while also promoting the apoptosis of colon epithelial cells induced by tumor-associated fibroblasts.[116] Similarly, Chlorogenic acid (extracted from Lonicerae) induces apoptosis of BC cells through the NF-κB signaling pathway.[117] In addition to inhibiting the expression of EMT proteins, Cinnamaldehyde (extracted from *Cinnamomum cassia*) has been found to induce apoptosis of non-small cell lung cancer (NSCLC) through the Wnt/β-catenin pathway.[85] Furthermore, several TCM-derived compounds induce apoptosis through cell cycle arrest. For example, ursolic acid (from Eriobotryae Folium) arrests the cell cycle at the G0/G1 phase, thereby triggering caspase-dependent apoptosis.[60] Similarly, Paris polyphylla ethanol extract induces G2/M arrest in bladder cancer cells and inhibits invasion, migration, and EMT of melanoma cells by activating autophagy.[118,119] Likewise, the root extract of Hemsleya amabilis Diels promotes apoptosis via G2/M arrest, modulates the expression of Bax and Bcl-2, and inhibits renal cell carcinoma cell proliferation through suppression of the PI3K/AKT signaling pathway.[96]

Participate in Metabolic Reprogramming

A study in NSCLC reported that in NSCLC A549 cells, the reconstructed mixture of baicalein, wogonin, and oroxylin-A was shown to inhibit EMT via modulation of the PI3K/Akt–TWIST1 axis, with proteomic evidence implicating suppression of the glycolytic pathway, suggesting a potential metabolic effect despite lacking direct mechanistic proof of metabolic reprogramming.[120] More compellingly, Oroxylin-A has been demonstrated to inhibit glycolysis-dependent proliferation in breast cancer by activating sirtuin 3 (SIRT3), destabilizing hypoxia inducible factor 1 subunit alpha (HIF-1α), and increasing superoxide dismutase 2 (SOD2) expression and activity, thereby providing concrete evidence of metabolic reprogramming by a TCM-derived compound.[121] Although direct evidence for the role of TCM in regulating ROS during EMT is currently lacking, some studies suggest that certain Chinese herbal extracts may affect tumor progression through ROS-mediated autophagy. For instance, the ethyl acetate extract of Biancaea sappan and a novel aniline derivative isolated from *Peganum harmala* L. have been shown to modulate tumor development by activating autophagy via ROS signaling.[122]

Discussion and Conclusion

Currently, the application of TCM in clinical oncology is both widespread and gaining increasing recognition, particularly in the prevention and management of tumor recurrence and metastasis. Research to date has demonstrated that TCM-derived compounds or individual constituents possess the capacity to impede the process of EMT and re-sensitize tumor cells to anoikis-induced apoptosis. These effects are mediated through the modulation of multiple biological processes, including tumor metabolism, ECM remodeling, transcription factor activity, signaling pathway regulation, and non-coding RNA expression. Therefore, targeting EMT and anoikis via TCM-based interventions represents a promising and novel research direction for limiting tumor invasion and metastasis.

However, current studies in this field face several limitations. Many investigations lack robust in vivo validation, such as the use of appropriate animal models, and fail to incorporate assessments of functional recovery or molecular interactions to substantiate mechanistic findings. Moreover, because most of the existing evidence is derived from in vitro experiments, animal studies, or investigations with relatively small sample sizes, substantial heterogeneity exists in study methodologies, dosing strategies, model selection, and outcome measurements. Such variability reduces the comparability across studies and may impose limitations on the interpretation of the results. In addition, some of the reported findings have yet to be validated in large-scale, rigorously designed clinical trials; therefore, the current conclusions should be interpreted with appropriate caution. To address these gaps, future research should adopt more rigorous and systematic approaches to elucidate the precise mechanisms underlying TCM's regulatory effects on EMT and anoikis. Moreover, identifying additional molecular targets and signaling pathways will further advance our understanding of how TCM can enhance tumor cell susceptibility to anoikis. These efforts will ultimately enrich the modern scientific foundation of TCM and support its role in suppressing tumor metastasis through evidence-based strategies.

Abbreviations

EMT, epithelial-mesenchymal transition; TCM, traditional Chinese medicine; ECM, extracellular matrix; MMPs, matrix metalloproteinases; TFs, transcription factors; ZEB1, zinc finger E-box binding homeobox 1; ZEB2, zinc finger E-box binding homeobox 2; SIP1, smad interacting protein 1; GSC, goosecoid; SIX1, SIX homeobox 1; FOXC2, forkhead box protein C2; α-SMA, α-smooth muscle actin; TGF-β, transforming growth factor-β; RREB1, ras responsive element binding protein 1; Trkb, tyrosine kinase receptor B; mRNA, messengerRNA; miRNA, microRNA; Lnc RNA-FOXD2-AS1, Long Noncoding RNA FOXD2 adjacent opposite strand RNA 1; STAT3, signal transducer and activator of transcription 3; ROCK2, Rho-associated coiled-coil containing protein kinase 2; lncRNA-SNHG12, Long Noncoding RNA small nucleolar RNA host gene 12; lncRNA-HOTAIR, Long Noncoding RNA HOX antisense intergenic RNA; lncRNA-LEF1-AS1, Long Noncoding RNA LEF1 antisense RNA 1; lncRNA-MEG3, Long Noncoding RNA maternally expressed gene 3; lncRNA-NEAT1, Long Noncoding RNA nuclear paraspeckle assembly transcript 1; lncRNA-TINCR, Long Noncoding RNA TINCR ubiquitin domain containing; MAPK, mitogen-activated protein kinase; ESCC, esophageal squamous cell carcinoma; ATF4, activating transcription factor 4; CRC, colorectal cancer; ROS, reactive oxygen species; ATP, adenosine triphosphate; PDK4, pyruvate dehydrogenase kinase 4; CEMIP, cell migration-inducing protein; PKCα, Protein Kinase C alpha; RAGE, advanced glycosylation End-Product specific receptor; DAMPs, damage-associated molecular patterns; NETs, neutrophil extracellular traps; BRSK2, BR serine/threonine kinase 2; ATG14, autophagy related 14; GSK-3, glycogen synthase kinase-3; NSCLC, non-small cell lung cancer; GC, gastric carcinoma; HCC, hepatocellular carcinoma; BC, breast cancer; TNBC, triple Negative Breast Cancer; SIRT3, sirtuin 3; SOD2, superoxide dismutase 2; HIF-1α, hypoxia inducible factor 1 subunit alpha.

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Disclosure

The authors declare that they have no competing interests.

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