

TCMVET Baituxiao

Academic Guide and Application Reference for Integrated Tumor Management in Dogs and Cats

Veterinary Academic Guide and Application Reference

For Veterinarians and Related Professionals

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Abstract

TCMVET Baituxiao is a professional herbal supplement developed from the traditional Chinese medicine principle of “supporting healthy qi and dispelling pathogenic factors.” This guide summarizes the academic rationale and practical reference points for its use in integrated tumor management in dogs and cats, covering traditional Chinese veterinary medicine theory, formula composition, preparation and quality-control processes, ingredient pharmacology, in vivo pharmacodynamic observations, and veterinary clinical application considerations.

This guide is intended for veterinarians and related professionals. It discusses the potential supportive role of Baituxiao in immune modulation, tumor-microenvironment management, treatment-tolerance support, quality-of-life maintenance, and long-term follow-up. Mechanistic data, animal-model findings, and real-world observational data cited in this document should be interpreted according to evidence tier. Findings from a single model or a single ingredient should not be treated as direct proof of clinical efficacy in dogs and cats.

Evidence Stratification and Reading Notes

This document is intended for veterinarians and related professionals. Terms related to treatment, efficacy, prevention, and disease are used in the context of veterinary academic exchange and clinical decision-making support. Evidence from single herbs, individual ingredients, in vitro experiments, mouse models, tumor-bearing dog models, real-world canine and feline cases, and clinical observations represents different levels of certainty and should be interpreted accordingly. No single model, ingredient, or exploratory case should be treated as confirmatory evidence for all canine and feline tumor cases.

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I. Formula Theory

Understanding of Pathogenesis in Traditional Chinese Medicine

According to this theory, the core pathogenesis of tumors arises from “deficiency of healthy qi, accumulation of heat-toxin, and interbinding of phlegm and blood stasis.” Specifically, when the body’s defense mechanism (healthy qi) is weakened, toxins (heat-toxin) accumulate and disrupt the normal circulation of qi, blood, and body fluids. This imbalance further leads to the formation of pathological products (phlegm and blood stasis), which ultimately congeal into masses.

Formula Principles and Strategy

In response to the above pathogenesis, four therapeutic methods are established: clearing heat and resolving toxicity, activating blood and dispelling stasis, transforming phlegm and dispersing nodules, and supporting healthy qi while consolidating the root. The formula follows the traditional “monarch-minister-assistant-courier” compatibility principle.

Detailed Description of Major Ingredients:

Hedyotis diffusa / *Oldenlandia diffusa* (commonly cited as *Hedyotis diffusa* Willd. / *Oldenlandia diffusa* (Willd.) Roxb.; accepted name often listed as *Scleromitron diffusum* (Willd.) R. J. Wang)

TCM theory: clears heat and resolves toxicity; activates blood and promotes dampness drainage

Key chemical components: ursolic acid and oleanolic acid (triterpenoids)

Modern pharmacological actions: activates the caspase protease family, induces the mitochondrial apoptotic pathway, inhibits the NF- κ B inflammatory signaling pathway, interrupts the tumor-associated chronic inflammatory microenvironment, suppresses the tumor-cell proliferation cycle, and arrests cells in the G0/G1 phase.

Astragalus (*Astragalus mongholicus* Bunge / *Astragalus membranaceus* (Fisch.) Bunge)

TCM theory: tonifies qi and secures the exterior; expels toxin and promotes tissue regeneration

Key chemical components: *Astragalus* polysaccharides and *Astragalus* saponins (astragaloside IV)

Modern pharmacological actions: activates immune cells such as macrophages and T lymphocytes, enhances nonspecific immune function, upregulates expression of the tumor suppressor protein p53, promotes DNA damage repair, alleviates chemotherapy-induced myelosuppression, and promotes hematopoietic stem-cell proliferation.

Scutellaria barbata (*Scutellaria barbata* D. Don)

TCM theory: clears heat and resolves toxicity; transforms stasis and promotes urination

Key chemical components: scutellarin and apigenin (flavonoids)

Modern pharmacological actions: inhibits vascular endothelial growth factor (VEGF) expression, blocks tumor angiogenesis, suppresses matrix metalloproteinase (MMP) activity, prevents tumor invasion and metastasis, induces G2/M cell-cycle arrest in tumor cells, and promotes apoptosis.

Rehmannia (*Rehmannia glutinosa* (Gaertn.) DC.)

TCM theory: clears heat and cools the blood; nourishes yin and generates fluids

Key chemical components: catalpol, verbascoside, and *Rehmannia* polysaccharides

Modern pharmacological actions: exerts notable anti-inflammatory and neuroprotective effects, reduces neuropathic pain, stimulates hematopoietic stem-cell proliferation, improves chemotherapy-induced myelosuppression, modulates immune function, and alleviates excessive inflammatory responses.

Angelica sinensis (*Angelica sinensis* (Oliv.) Diels)

TCM theory: nourishes and activates blood; regulates menstruation and relieves pain

Key chemical components: ferulic acid and ligustilide (volatile oil constituent)

Modern pharmacological actions: provides strong antioxidant activity, scavenges free radicals, reduces oxidative injury, improves microcirculation, increases drug perfusion in tumor tissues, modulates immune function, and promotes lymphocyte activation.

Atractylodes macrocephala (*Atractylodes macrocephala* Koidz.)

TCM theory: strengthens the spleen and tonifies qi; dries dampness and promotes water metabolism

Key chemical components: atractylenolides I, II, and III, and atractylon

Modern pharmacological actions: regulates gastrointestinal motility, improves appetite, alleviates cachexia, induces autophagy in tumor cells, promotes clearance of abnormal cells, modulates immunity, and enhances disease resistance.

Paris polyphylla (*Paris polyphylla* Sm.)

TCM theory: clears heat and resolves toxicity; reduces swelling and relieves pain

Key chemical components: steroidal saponins (polyphyllins I, II, and VII)

Modern pharmacological actions: exerts direct cytotoxic effects, disrupts tumor-cell membrane structure, induces cell-cycle arrest, prevents tumor-cell division, regulates expression of apoptosis-related proteins, and promotes tumor-cell apoptosis.

Curcuma phaeocaulis (*Curcuma phaeocaulis* Valetton)

TCM theory: breaks blood stasis and moves qi; disperses accumulation and relieves pain

Key chemical components: curcuminol, beta-elemene, and curcumin

Modern pharmacological actions: induces tumor-cell apoptosis through the mitochondrial pathway, inhibits tumor angiogenesis, blocks nutritional supply, exerts anti-inflammatory and antioxidant effects, and reduces inflammation in the tumor microenvironment.

Prunella vulgaris (*Prunella vulgaris* L.)

TCM theory: clears liver heat and drains fire; disperses nodules and reduces swelling

Key chemical components: rosmarinic acid and *Prunella* saponins

Modern pharmacological actions: inhibits inflammatory factor expression, improves the tumor microenvironment, induces tumor-cell cycle arrest and apoptosis, modulates immune function, and enhances antitumor immunity.

Red peony root (*Paeonia lactiflora* Pall. / *Paeoniae Radix Rubra*)

TCM theory: clears heat and cools the blood; disperses stasis and relieves pain

Key chemical components: monoterpene glycosides such as paeoniflorin and albiflorin

Modern pharmacological actions: anti-inflammatory and analgesic effects, reduction of tumor-related pain, improvement in microcirculation and tissue oxygenation, immune modulation, and regulation of inflammatory-factor balance.

Spatholobus stem (*Spatholobus suberectus* Dunn / *Spatholobi Caulis*)

TCM theory: activates and nourishes blood; relaxes sinews and unblocks collaterals

Key chemical components: catechins (epicatechin) and flavonoids

Modern pharmacological actions: improves hemorheology, inhibits platelet aggregation, provides antioxidant activity, reduces oxidative-stress injury, promotes hematopoiesis, and improves anemia status.

Ranunculus ternatus (*Ranunculus ternatus* Thunb.)

TCM theory: transforms phlegm and disperses nodules; resolves toxicity and reduces swelling

Key chemical components: saponins and polysaccharides

Modern pharmacological actions: enhances immune-cell activity, increases phagocytic function, directly inhibits tumor-cell proliferation, exerts anti-inflammatory and anti-allergic effects, and regulates immune balance.

Shancigu (*Cremastra appendiculata* (D. Don) Makino / *Pleione bulbocodioides* (Franch.) Rolfe and related botanical sources)

TCM theory: clears heat and resolves toxicity; transforms phlegm and disperses nodules

Key chemical components: colchicine derivatives and phenanthrene compounds

Modern pharmacological actions: inhibits tubulin polymerization, prevents mitosis, induces tumor-cell apoptosis, and suppresses tumor angiogenesis.

Dandelion (*Taraxacum mongolicum* Hand.-Mazz. / *Taraxacum officinale* F. H. Wigg.)

TCM theory: clears heat and resolves toxicity; reduces swelling and disperses nodules

Key chemical components: taraxasterol, taraxacin, and flavonoids

Modern pharmacological actions: induces tumor-cell apoptosis, provides antioxidant activity, scavenges free radicals, promotes bile flow, supports liver protection, and facilitates toxin excretion.

Poria / *Wolfiporia* (*Wolfiporia cocos* (F. A. Wolf) Ryvarden & Gilb.; formerly *Poria cocos*)

TCM theory: promotes urination and leaches dampness; strengthens the spleen and calms the spirit

Key chemical components: beta-Poria polysaccharides and Poria triterpenes (pachymic acid)

Modern pharmacological actions: immune modulation, enhancement of cellular immunity, direct cytotoxic action on tumor cells, diuretic and sedative effects, and improvement in clinical signs.

Honeysuckle flower (*Lonicera japonica* Thunb.)

TCM theory: clears heat and resolves toxicity; disperses wind-heat

Key chemical components: chlorogenic acid and luteoloside

Modern pharmacological actions: broad-spectrum antibacterial and antiviral activity, inhibition of tumor-cell proliferation, antioxidant effects, and reduction of oxidative injury.

Gardenia fruit (*Gardenia jasminoides* J. Ellis / *Gardeniae Fructus*)

TCM theory: drains fire and relieves irritability; clears heat and promotes dampness drainage

Key chemical components: geniposide

Modern pharmacological actions: hepatoprotective and choleric effects, promotion of toxin metabolism, anti-inflammatory and antioxidant actions, reduction of tissue injury, sedative and analgesic effects, and improvement in clinical signs.

Thunberg fritillary bulb (*Fritillaria thunbergii* Miq. / *Fritillariae Thunbergii Bulbus*)

TCM theory: clears heat and transforms phlegm; disperses nodules and resolves abscesses

Key chemical components: peimine (verticine) and peiminine (verticinone)

Modern pharmacological actions: relieves cough, transforms phlegm, improves respiratory signs, reverses multidrug resistance in tumors, and directly inhibits tumor-cell proliferation.

Sparganium rhizome (*Sparganium stoloniferum* Buch.-Ham. ex Graebn.)

TCM theory: breaks blood stasis and moves qi; disperses accumulation and relieves pain

Key chemical components: volatile oils, flavonoids, and phenylpropanoids

Modern pharmacological actions: improves hemorheology, inhibits thrombosis, suppresses tumor-cell proliferation, provides anti-inflammatory and analgesic effects, and improves clinical signs.

Arnebia euchroma / Xinjiang gromwell (*Arnebia euchroma* (Royle) I. M. Johnst.)

TCM theory: clears heat and cools blood; activates blood and resolves toxicity

Key chemical components: shikonin and acetylshikonin

Modern pharmacological actions: inhibits topoisomerase, causes DNA damage, induces tumor-cell apoptosis, and provides anti-inflammatory and antibacterial activity while reducing infection-related risk.

Chuanxiong (*Ligusticum chuanxiong* Hort. ex S. H. Qiu, Y. Q. Zeng, K. Y. Pan, Y. C. Tang & J. M. Xu)

TCM theory: activates blood and moves qi; dispels wind and relieves pain

Key chemical components: ligustrazine, ferulic acid, and ligustilide

Modern pharmacological actions: improves microcirculation, increases tissue perfusion, inhibits platelet aggregation, helps prevent thrombosis, provides analgesic and anti-inflammatory effects, and reduces pain signs.

Notoginseng (*Panax notoginseng* (Burkill) F. H. Chen)

TCM theory: disperses stasis and stops bleeding; reduces swelling and relieves pain

Key chemical components: notoginsenoside R1 and ginsenosides Rg1 and Rb1

Modern pharmacological actions: promotes hematopoiesis, improves anemia status, inhibits thrombosis, improves microcirculation, modulates immunity, and enhances host resistance.

Eclipta (*Eclipta prostrata* (L.) L.)

TCM theory: nourishes the liver and kidney; cools blood and stops bleeding

Key chemical components: wedelolactone and thiophene compounds

Modern pharmacological actions: protects the liver, promotes bile flow, facilitates toxin excretion, modulates and enhances immune function, provides antioxidant activity, and reduces oxidative injury.

Licorice (*Glycyrrhiza uralensis* Fisch. ex DC. / *Glycyrrhiza glabra* L.)

TCM theory: tonifies the spleen and qi; clears heat and resolves toxicity

Key chemical components: glycyrrhizic acid, glycyrrhetic acid, and licorice flavonoids

Modern pharmacological actions: hormone-like anti-inflammatory effects, immune modulation, balancing of immune function, detoxifying and hepatoprotective effects, and reduction of drug toxicity.

Salvia chinensis (*Salvia chinensis* Benth.)

TCM theory: clears heat and resolves toxicity; activates blood and relieves pain

Key chemical components: flavonoids, phenolic acids, and diterpenes

Modern pharmacological actions: induces tumor-cell apoptosis, inhibits tumor-cell proliferation, provides anti-inflammatory and antioxidant effects, and improves the microenvironment.

Schisandra (*Schisandra chinensis* (Turcz.) Baill.)

TCM theory: astringes and consolidates; tonifies qi and generates fluids

Key chemical components: lignans

Modern pharmacological actions: antioxidant activity, reduction of oxidative injury, hepatoprotective and detoxification support, promotion of toxin metabolism, immune modulation, and enhancement of disease resistance.

Ginseng (*Panax ginseng* C. A. Mey.)

TCM theory: strongly tonifies primordial qi; restores the pulse and prevents collapse

Key chemical components: ginsenosides (Rg3, Rh2, Rb1)

Modern pharmacological actions: immune modulation, enhancement of immune function, anti-fatigue effects, improvement in quality of life, and induction of tumor-cell differentiation and apoptosis.

Reishi / Lingzhi (*Ganoderma lucidum* (Curtis) P. Karst.)

TCM theory: tonifies qi and calms the spirit; stops cough and relieves wheezing

Key chemical components: *Ganoderma* polysaccharides and *Ganoderma* triterpenes

Modern pharmacological actions: immune modulation, activation of immune cells, direct inhibition of tumor-cell proliferation, antioxidant activity, and reduction of treatment-related adverse effects.

Turkey tail / Yun-zhi (*Trametes versicolor* (L.) Lloyd; syn. *Coriolus versicolor* (L.) Quél.)

TCM theory: strengthens the spleen and promotes dampness drainage

Key chemical components: polysaccharide-K (PSK) and polysaccharopeptide (PSP) from Turkey tail

Modern pharmacological actions: immune modulation, enhancement of immune function, direct antitumor activity, and reduction of adverse effects from radiotherapy and chemotherapy.

Note: This product formula also contains additional undisclosed natural ingredients and carefully selected compatible components. As part of trade-secret and proprietary processing technology, these components are intended to optimize overall efficacy and stability through more complex synergistic effects, and their value is reflected in the final product effect.

II. Preparation Process and Quality Control

2.1 Raw Material Sources, Wild/Wild-Simulated Attributes, Dao-Di Authenticity, and Quality Control

All botanical raw materials used in this study were selected according to the principles of Dao-di medicinal materials and internal raw-material selection standards, with priority given to wild or wild-simulated materials from traditional Dao-di production areas rather than ordinary cultivated materials. Selection focused on botanical origin, geographic source, ecological environment of the production area, growth mode, harvest season, medicinal part, primary processing method, appearance, odors, and the presence or absence of mold, insect damage, adulteration, substitution, or other quality abnormalities. Batch source records were established for all selected raw materials to ensure traceability of origin, harvest, primary processing, and warehousing.

To reduce the potential impact of source variation in natural medicinal materials on preparation quality and subsequent pharmacodynamic evaluation, this study established a source-stratified Dao-di quality-control strategy. Wild, wild-simulated, and ordinary cultivated materials were evaluated as different source tiers. Ordinary cultivated materials primarily served as comparator samples for analyzing differences from wild and wild-simulated materials in

macroscopic characteristics, microscopic features, chromatographic fingerprints, contents of major marker constituents, and safety indicators.

This study did not simply use “wild” or “wild-simulated” status as the basis for judging quality. Instead, through source-stratified comparison, it experimentally examined whether Dao-di production areas, ecological growth conditions, and traditional harvest methods were associated with the quality attributes required for this compound formula. Quality evaluation included macroscopic identification, microscopic identification, chromatographic fingerprint similarity analysis, determination of major marker constituents, moisture, ash, extract content, and safety testing for heavy metals, pesticide residues, microbial limits, mycotoxins, and sulfur dioxide residues as required by the type of material and relevant quality-attribute standards.

Regarding raw-material release standards, only batches meeting the predetermined botanical origin, Dao-di source characteristics, wild or wild-simulated source requirements, fingerprint consistency, and internal quality standards could proceed to extraction and preparation. This raw-material control approach was integrated with subsequent extraction, concentration, drying, and finished-product testing to form a full-process quality-control system from raw-material sourcing to final preparation. Through source-stratified comparison, Dao-di verification, multi-marker constituent control, and safety evaluation, this study improved the scientific basis for raw-material selection, batch-to-batch quality stability, and reproducibility of subsequent research findings.

Unlike traditional raw-material quality control, which mainly relies on botanical identification and measurement of one or a few marker components, this study incorporated raw-material source, wild/wild-simulated attributes, and Dao-di authenticity into a unified quality-evaluation framework. Ordinary cultivated materials were used as comparative controls to establish a source-stratified Dao-di quality-control strategy, thereby defining an acceptable raw-material quality range for this compound preparation and improving the quality foundation and interpretability of subsequent pharmacodynamic evaluation.

2.2 Objectives and Evaluation Indicators for Process Optimization

Baituxiao is a multi-herb traditional Chinese veterinary compound formula. Its raw materials include botanical medicines, animal-derived materials, and harder mineral/shell materials. Different materials vary in water absorption, release rate of active components, and thermal stability. To improve the overall transfer rate of the active substance group in the finished compound formula and ensure batch-to-batch stability of the capsule dosage form, dry extract yield, solid content, marker-constituent content, fingerprint similarity, concentration efficiency, spray-drying compatibility, capsule-filling stability, and batch consistency are recommended as core indicators for process screening.

After process optimization, the recommended standardized preparation route for the finished Baituxiao compound formula is “soaking in five-fold volume of water - five consecutive decoction extractions - combining filtrates - vacuum concentration - spray drying - capsule formation.” The purpose of this process is not simply to increase extraction frequency, but to establish a controllable, verifiable, and scalable preparation procedure for a multi-ingredient, complex-matrix formula intended for long-term administration.

2.3 Water Extraction and Five-Decoction Extraction Process

The specific process is as follows: each raw material is weighed according to the prescription ratio, cleaned, impurities removed, dried, pulverized, passed through a 20-mesh sieve, and mixed; purified water equivalent to approximately five times the total weight of the medicinal materials is added, followed by soaking for 30 minutes to allow full water absorption and swelling; five consecutive decoction extractions are performed, each for approximately 60 minutes, and the hot filtrates are combined; the combined filtrate is concentrated under reduced pressure, with the concentration endpoint controlled at a clear extract with a relative density of approximately 1.10-1.20 at 60 °C; the clear extract is spray-dried to obtain dry extract powder, followed by granulation and hard-capsule filling.

The technical rationale for five consecutive decoctions is as follows. First, it can improve the overall extraction rate of polysaccharides, flavonoids, saponins, and other water-soluble small molecules. Second, it accommodates the release characteristics of materials with different textures, such as *Hedyotis diffusa*, *Scutellaria barbata*, *Astragalus*, and *Poria*. Third, compared with a single prolonged high-temperature decoction, fractional extraction helps reduce losses of certain heat-sensitive components caused by prolonged heating. Fourth, combining multiple filtrates can balance batch differences in water absorption and release efficiency, improving the consistency of extract solid content and marker components.

2.4 Capsule Formation and Quality Control

After sieving, the dry extract powder is combined with palatability excipients and necessary formulation excipients. After mixing, granulation, low-temperature drying, and particle sizing, it is filled into hard capsules. Key quality controls for the capsule should include fill-weight variation, disintegration time, moisture, microbial limits, heavy metals, pesticide residues, aflatoxins, marker-constituent content, and batch-to-batch stability.

2.5 Marker Constituents and Process Verification

Astragalus polysaccharides, ginsenoside-related components, total flavonoids or related phenolic acids from *Hedyotis diffusa*, total *Panax notoginseng* saponins, and compound-formula fingerprint similarity are used as core quality-evaluation indicators. Subsequent testing systems may be established using HPLC, UPLC, HPLC-ELSD, or LC-MS, and comparison of two-, three-, four-, five-, and six-decoction protocols may verify the rationality of five extractions in terms of constituent transfer rate, dry extract yield, and energy-cost balance.

Table 1. Quality-Control Levels and Veterinary Professional Significance

Quality-control level	Recommended control items	Veterinary professional significance
Raw medicinal materials	Botanical-origin identification, heavy metals, pesticide residues, aflatoxins, microbial limits	Reduce source variation and safety risks of raw materials
Intermediate	Relative density, solids, dry extract yield, marker components, fingerprint	Confirm controllability of extraction and concentration processes
Finished capsule	Fill-weight variation, disintegration, moisture, microbiology, stability, batch-to-batch consistency	Ensure clinical-use dosage and product stability

III. Major Mechanisms of Action and Evidence Levels

The mechanisms of action of this product are based on a synergistic concept of “multiple components - multiple targets - multiple pathways.” The following sections describe each module in detail and assess evidence levels according to current research evidence. Evidence levels are classified with reference to international practice as follows: Grade A (strong), supported by multiple well-designed preclinical studies or preliminary clinical data; Grade B (moderate), supported by some in vitro or animal experimental data but with limited clinical evidence; and Grade C (theoretical), primarily based on traditional theory, known pharmacological inference of components, and preliminary research suggesting potential effects. The A/B/C grading in this document mainly reflects the strength of mechanistic support and consistency of data, and is not equivalent to clinical efficacy evidence levels for the finished compound formula in dogs and cats.

Immune-System Modulation Mechanisms

Overall description: activates and regulates innate and adaptive immunity through multiple pathways, reverses the immunosuppressive state in the tumor microenvironment (TME), and enhances immune surveillance and clearance capacity.

Table 2. Immune-System Modulation Mechanisms and Representative Constituents

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Activation of innate immunity	Acts as a high-affinity agonist of Toll-like receptor 4 (TLR4), activating the TAK1 complex through the TLR4/MyD88/IRAK/TRAF6 signaling axis and thereby driving NF-kappaB and MAPK signaling pathways. This promotes M1 polarization of macrophages, upregulates pro-inflammatory factors such as iNOS, COX-2, TNF-alpha, IL-1beta, and IL-6, and enhances phagocytic activity. It also significantly increases NK-cell cytotoxicity.	Astragalus polysaccharide (arabinogalactan, AG)	Grade A

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Activation of innate immunity	Polysaccharides: synergistically activate TLR4 and Dectin-1 receptors. Dectin-1 activates the Syk/CARD9 pathway and cross-talks with TLR4 signaling, strongly amplifying NF-kappaB and IRF pathway activation and inducing robust type I interferon responses and cytokine production. Triterpenes: indirectly activate the NLRP3 inflammasome by inducing reactive oxygen species generation and mitochondrial dysfunction, promoting caspase-1-mediated maturation of IL-1beta and IL-18.	Reishi/Lingzhi polysaccharides (β -(1 \rightarrow 3)-D-glucan), Reishi/Lingzhi triterpenes (e.g., ganoderic acids)	Grade A
Activation of innate immunity	Immune receptor activation: can be recognized by receptors such as dendritic-cell-associated C-type lectin-1 (Dectin-1), inducing a strong type I interferon response through the Syk/IRF5 pathway. Complement activation: acts as an activating surface and directly activates the complement system through the alternative pathway, generating the anaphylatoxins C3a and C5a and strongly chemotaxing and activating neutrophils and macrophages. Nonspecific stimulation: broadly enhances phagocytosis and respiratory burst capacity of macrophages and neutrophils.	Turkey tail polysaccharide-K (proteoglycan, PSK)	Grade A
Activation of innate immunity	Polysaccharides: activate the NF-kappaB pathway through pattern-recognition receptors such as TLR4, promoting macrophage activation and cytokine secretion, while the effect is relatively mild and reflects bidirectional regulation. Ferulic acid: as a histone deacetylase (HDAC) inhibitor, it relaxes chromatin through epigenetic mechanisms (increased histone acetylation), enhances accessibility of immune-related genes to transcription factors, and has a "sensitizing" effect.	Angelica sinensis polysaccharide (fructogalactan), ferulic acid (phenylpropanoid)	Grade A
Activation of innate immunity	Saponin Rg1: as a functionally selective ligand of the glucocorticoid receptor (GR), it mediates partial anti-inflammatory effects while not inhibiting and even synergistically enhancing NF-kappaB transcriptional activity. It activates the AMPK pathway and drives fatty-acid oxidation in macrophages, providing energy support for M1 polarization (immunometabolic reprogramming). Polysaccharides: directly activate macrophages through receptors such as TLR4.	total Panax notoginseng saponins (e.g., ginsenoside Rg1), Panax notoginseng polysaccharide	Grade A
Activation of innate immunity	A classic TLR4 agonist. It activates macrophages through the TLR4/NF-kappaB pathway, enhancing phagocytosis, nitric oxide (NO) and reactive oxygen species (ROS) production, and secretion of pro-inflammatory cytokines. Its linear beta-glucan structure can form a triple-helix conformation with good receptor affinity.	Poria/Wolfiporia polysaccharides (β -(1 \rightarrow 3)-D-glucan)	Grade A

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Activation of innate immunity	Multi-target regulation: ginsenosides may rapidly activate PI3K/Akt and eNOS pathways through interactions with G protein-coupled receptors (GPCRs) or ion channels. They also modulate MAPK and NF-kappaB signaling and enhance the activity and cytotoxicity of NK cells and macrophages. Different ginsenosides, such as Rg1 and Rb1, may contribute to bidirectional immune regulation.	ginsenoside (e.g., Rg1, Rb1)	Grade A

Table 2 (continued). Immune-System Modulation Mechanisms and Representative Constituents

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Regulation of adaptive immunity	Precisely regulates adaptive immune responses by modulating the differentiation and function of T-lymphocyte subsets (such as Th1, Th2, Th17, Treg, and CTL), as well as B-lymphocyte activation and antibody production. The core lies in bidirectional regulation to maintain immune homeostasis rather than simple enhancement. For example, the effects of Ginseng and Astragalus are context-dependent, whereas Licorice and Schisandra tend toward immunosuppression to address excessive immune responses.	schizandrin (lignans, e.g., schisandrin B)	Grade A
Regulation of adaptive immunity	Precisely regulates adaptive immune responses by modulating the differentiation and function of T-lymphocyte subsets (such as Th1, Th2, Th17, Treg, and CTL), as well as B-lymphocyte activation and antibody production. The core lies in bidirectional regulation to maintain immune homeostasis rather than simple enhancement. For example, the effects of Ginseng and Astragalus are context-dependent, whereas Licorice and Schisandra tend toward immunosuppression to address excessive immune responses.	glycyrrhizic acid, glycyrrhetic acid	Grade A
Regulation of adaptive immunity	Precisely regulates adaptive immune responses by modulating the differentiation and function of T-lymphocyte subsets (such as Th1, Th2, Th17, Treg, and CTL), as well as B-lymphocyte activation and antibody production. The core lies in bidirectional regulation to maintain immune homeostasis rather than simple enhancement. For example, the effects of Ginseng and Astragalus are context-dependent, whereas Licorice and Schisandra tend toward immunosuppression to address excessive immune responses.	ginsenoside (e.g., Rg1, Rb1, Rg3)	Grade A
Regulation of adaptive immunity	Precisely regulates adaptive immune responses by modulating the differentiation and function of T-lymphocyte subsets (such as Th1, Th2, Th17, Treg, and CTL), as well as B-lymphocyte activation and antibody production. The core lies in bidirectional regulation to maintain immune homeostasis rather than simple enhancement. For example, the effects of Ginseng and Astragalus are context-dependent, whereas Licorice and Schisandra tend toward immunosuppression to address excessive immune responses.	Turkey tail polysaccharide-K (PSK)	Grade A

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Regulation of adaptive immunity	Precisely regulates adaptive immune responses by modulating the differentiation and function of T-lymphocyte subsets (such as Th1, Th2, Th17, Treg, and CTL), as well as B-lymphocyte activation and antibody production. The core lies in bidirectional regulation to maintain immune homeostasis rather than simple enhancement. For example, the effects of Ginseng and Astragalus are context-dependent, whereas Licorice and Schisandra tend toward immunosuppression to address excessive immune responses.	Reishi/Lingzhi polysaccharides, Reishi/Lingzhi glycopeptides	Grade A
Regulation of adaptive immunity	Precisely regulates adaptive immune responses by modulating the differentiation and function of T-lymphocyte subsets (such as Th1, Th2, Th17, Treg, and CTL), as well as B-lymphocyte activation and antibody production. The core lies in bidirectional regulation to maintain immune homeostasis rather than simple enhancement. For example, the effects of Ginseng and Astragalus are context-dependent, whereas Licorice and Schisandra tend toward immunosuppression to address excessive immune responses.	Astragalus polysaccharide, astragaloside	Grade A
Regulation of cytokine networks	Regulatory effects on cytokine networks	Constituents	Evidence level

Table 2 (continued). Immune-System Modulation Mechanisms and Representative Constituents

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Regulation of cytokine networks	Research suggests effects on secretion of Th1-type cytokines such as IL-2 and IFN-gamma	Scutellaria barbata	Grade C
Regulation of cytokine networks	Research suggests modulation of cytokine levels such as IL-2, IL-12, and TNF-alpha	Hedyotis diffusa	Grade C
Regulation of cytokine networks	Downregulates pro-inflammatory factors (TNF-alpha, IFN-gamma) in autoimmune models	Rehmannia	Grade B
Regulation of cytokine networks	Downregulates pro-inflammatory factors (TNF-alpha, IL-6) and regulates Th1/Th2 balance	Schisandra	Grade B
Regulation of cytokine networks	Strongly induces macrophages to produce pro-inflammatory factors such as TNF-alpha and IL-6	Paris polyphylla	Grade B
Regulation of cytokine networks	Downregulates pro-inflammatory factors (TNF-alpha, IL-6, IL-1beta, IL-8) through the NF-kappaB/MAPK pathway	Prunella vulgaris	Grade B
Regulation of cytokine networks	Inhibits overexpression of tumor-promoting factors (TNF-alpha, IL-6) in the tumor microenvironment	Panax notoginseng	Grade B
Regulation of cytokine networks	Potently inhibits the NF-kappaB pathway and downregulates pro-inflammatory factors (TNF-alpha, IL-6, IL-1beta)	Licorice	Grade A
Regulation of cytokine networks	Downregulates immunosuppressive factors (TGF-beta, IL-10) and upregulates antitumor factors (IFN-gamma, IL-12, TNF-alpha)	Reishi/Lingzhi	Grade A

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Regulation of cytokine networks	Downregulates immunosuppressive factors (TGF-beta, IL-10) and tumor-promoting factors (IL-6, IL-8), and upregulates immune-activating factors (IL-2, IFN-gamma)	Turkey tail	Grade A
Improvement of the tumor microenvironment	Specific mechanism	Major components	Grade A
Improvement of the tumor microenvironment	The specific three-dimensional helical structure of polysaccharides and the type of glycosidic bonds determine the specificity with which they are recognized by immune receptors. The amphipathic nature of saponins allows them to insert into cell membranes, while their aglycone structures and glycosylation patterns determine target selectivity and intensity. The hydrophobicity of terpenoids facilitates their entry into cells to regulate enzyme activity and signaling pathways. Phenolic substances such as flavonoids, lignans, and phenolic acids possess conjugated systems and phenolic hydroxyl groups that provide strong antioxidant capacity and allow binding to enzyme active sites through hydrogen bonding and hydrophobic interactions, thereby inhibiting key inflammatory signaling pathways such as NF-kappaB. In brief, specific chemical structures constitute the molecular basis by which these components can precisely regulate the tumor microenvironment.	Through the combined actions of Scutellaria barbata, Hedyotis diffusa, Schisandra, Prunella vulgaris, Paris polyphylla, Licorice, Ginseng, Curcuma phaeocaulis, Panax notoginseng, Astragalus, Reishi, and Turkey tail, the tumor microenvironment is effectively improved.	Grade A

Mechanisms Directly Inhibiting Tumor Cells

Overall description: inhibits malignant biological behaviors of tumor cells through multiple direct pathways, inducing cell death or loss of proliferative capacity.

Table 3. Mechanisms Directly Inhibiting Tumor Cells

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Induction of apoptosis	Activates the caspase-8/9/3 cascade, regulates the Bax/Bcl-2 ratio, and induces the mitochondrial apoptotic pathway.	Paris polyphylla: polyphyllin VII (steroidal saponins)	Grade A
Induction of apoptosis	Induces apoptosis through ROS-mediated JNK/p38 MAPK signaling and inhibits the PI3K/Akt survival pathway.	Arnebia euchroma: shikonin (naphthoquinone class)	Grade A
Induction of apoptosis	Activates caspase-3/9 and regulates the DR4/DR5 death-receptor pathway to induce extrinsic apoptosis.	Curcuma phaeocaulis: beta-elemene (sesquiterpenoids)	Grade A
Induction of apoptosis	Acts through a p53-dependent apoptotic pathway and inhibits survivin expression.	Sparganium rhizome: total Sparganium flavonoids (flavonoids)	Grade B
Induction of apoptosis	Regulates the Bax/Bcl-2 ratio, activates caspase-3, and induces ROS production.	Hedyotis diffusa: asperuloside (iridoid)	Grade B

Table 3 (continued). Mechanisms Directly Inhibiting Tumor Cells

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Induction of apoptosis	Induces CHOP expression through the endoplasmic-reticulum stress pathway and activates caspase-12.	Reishi/Lingzhi: ganoderic acid A (triterpenes)	Grade B

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Induction of apoptosis	Can induce cancer-cell apoptosis through both the mitochondrial pathway (downregulating Bcl-2, upregulating Bax, and activating caspase-9/3) and the death-receptor pathway (activating caspase-8/3).	Dandelion: taraxa sterol and related sterols, taraxerol, chlorogenic acid, caffeic acid, luteolin, apigenin, inulin	Grade A
Induction of cell-cycle arrest	Arrests the cell cycle in G2/M phase and inhibits CDK1/Cyclin B1 complex activity.	Shancigu (<i>Cremastra appendiculata</i> / <i>Pleione bulbocodioides</i>): phenanthrene and bibenzyl compounds (e.g., erianin)	Grade B
Induction of cell-cycle arrest	Arrests the cell cycle in G1 phase and downregulates Cyclin D1/CDK4/6 expression.	Fritillaria thunbergii bulb: peimine (steroidal alkaloid)	Grade A
Induction of cell-cycle arrest	Induces G0/G1-phase arrest and upregulates the cyclin-dependent kinase inhibitor p21.	Panax notoginseng: ginsenoside Rg3 and notoginsenoside R1 (dammarane-type triterpenoid saponins)	Grade B
Induction of cell-cycle arrest	Induces G1-phase arrest through regulation of the pRb-E2F pathway.	Ginseng: ginsenoside Rb1, Rg1 (dammarane-type triterpenoid saponins)	Grade B
Induction of cell-cycle arrest	Total saponins can arrest the cell cycle in G0/G1 phase, likely through regulation of cell-cycle proteins such as Cyclin D1 and CDKs.	Ranunculus ternatus: saponins	Grade B
Inhibition of tumor stem cells	Inhibits the Wnt/ β -catenin pathway and downregulates stem-cell markers such as CD44 and CD133.	Astragalus: astragaloside (cycloartane-type triterpenoid saponin)	Grade B
Inhibition of tumor stem cells	Inhibits Notch and Hedgehog signaling pathways and reduces tumor-sphere formation capacity.	Ginseng: ginsenoside Rh2, Rg3 (dammarane-type triterpenoid saponins)	Grade B
Inhibition of tumor stem cells	Inhibits tumor-stem-cell self-renewal through regulation of microRNAs such as miR-145.	glycyrrhetic acid (oleanane-type triterpene)	Grade C
Induction of autophagic cell death	Induces autophagic flux through the AMPK/mTOR pathway; at high concentrations, this may lead to autophagic cell death.	Reishi/Lingzhi: Reishi/Lingzhi polysaccharides (β -glucan)	Grade B
Induction of autophagic cell death	Induces mitophagy through activation of BNIP3 and promotes autophagic flux.	Turkey tail polysaccharide-K (PSK) (proteoglycan)	Grade B

C. Mechanisms Inhibiting Tumor Metastasis and Angiogenesis

Overall description: blocks key steps involved in tumor invasion, migration, and establishment of new blood supply.

Table 4. Mechanisms Inhibiting Tumor Metastasis and Angiogenesis

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Anti-angiogenesis / inhibition of tumor neovascularization	Potently inhibits the expression of vascular endothelial growth factor (VEGF) and its receptor VEGFR-2, thereby blocking downstream PI3K/Akt signaling.	Curcuma phaeocalis: β -elemene (sesquiterpenoid compound)	Grade A
Anti-angiogenesis / inhibition of tumor neovascularization	Specifically inhibits VEGF-induced endothelial-cell migration and proliferation and downregulates hypoxia-inducible factor-1 α (HIF-1 α).	Ginseng: ginsenoside Rg3 (dammarane-type triterpenoid saponins)	Grade A
Anti-angiogenesis / inhibition of tumor neovascularization	Its active component Rg3 is a recognized inhibitor of VEGF signaling. Total Panax notoginseng saponins may significantly reduce microvessel density (MVD) in tumor tissue.	Panax notoginseng: ginsenoside Rg3 and notoginsenoside R1 (dammarane-type triterpenoid saponins)	Grade A
Anti-angiogenesis / inhibition of tumor neovascularization	Preliminary in vitro studies suggest that its extract may inhibit endothelial-cell proliferation and tube formation. This activity may be related to anti-inflammatory and antioxidant effects, although specific molecular targets and pathways require further clarification.	Scutellaria barbata: flavonoids (e.g., scutellarin), clerodane diterpenoids	Grade C

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Inhibition of invasion and metastasis (blocking cancer-cell spread)	Significantly downregulates the activity and expression of matrix metalloproteinases MMP-2 and MMP-9, while upregulating their inhibitors TIMP-1 and TIMP-2.	Paris polyphylla: steroidal saponins (e.g., polyphyllin VII)	Grade A

Table 4 (continued). Mechanisms Inhibiting Tumor Metastasis and Angiogenesis

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Inhibition of invasion and metastasis (blocking cancer-cell spread)	Its extract may reduce cancer-cell invasion and migration by inhibiting MMP-2 and MMP-9 protein expression.	Hedyotis diffusa: total flavonoid (e.g., quercetin), asperuloside (iridoid glycoside)	Grade B
Inhibition of invasion and metastasis (blocking cancer-cell spread)	May block epithelial-mesenchymal transition (EMT) by inhibiting MMP-2/9 expression and NF-κB signaling.	Licorice: glycyrrhetic acid (oleanane-type pentacyclic triterpene)	Grade B
Inhibition of invasion and metastasis (blocking cancer-cell spread)	Its flavonoid components may upregulate E-cadherin, downregulate N-cadherin, and reverse epithelial-mesenchymal transition (EMT). They may also inhibit MMP-2/9 expression, thereby reducing cancer-cell invasion and migration.	Dandelion: flavonoids (e.g., luteolin)	Grade A
Improvement of hypercoagulability and inhibition of tumor-cell adhesion	Improves hypercoagulability by inhibiting platelet-derived growth factor (PDGF) expression, reducing platelet aggregation, lowering blood viscosity, and improving tumor microcirculation. By improving microcirculation, it may indirectly reduce cancer-cell adhesion and seeding on the vascular wall.	Chuanxiong: ligustrazine (tetramethylpyrazine, alkaloids)	Grade A
Improvement of hypercoagulability and inhibition of tumor-cell adhesion	Improves hypercoagulability through antiplatelet and fibrinolysis-promoting effects and may significantly improve hemorheology. It may also reduce thrombus-assisted adhesion of circulating tumor cells during hematogenous metastasis.	Panax notoginseng: total Panax notoginseng saponins (PNS) (mixture of dammarane-type triterpenoid saponins)	Grade A
Improvement of hypercoagulability and inhibition of tumor-cell adhesion	Ferulic acid can inhibit thromboxane A2 (TXA2) generation in platelets and reduce platelet aggregation. It may help improve the hypercoagulable state commonly seen in tumor patients and support microcirculation. By enhancing immune clearance of circulating tumor cells, it may reduce opportunities for adhesion; however, molecular evidence for direct inhibition of tumor-cell/endothelial adhesion molecules such as ICAM-1 and VCAM-1 remains limited.	Angelica sinensis: ferulic acid (phenolic acid-class compound)	Grade C
Improvement of hypercoagulability and inhibition of tumor-cell adhesion	Studies suggest some antiplatelet and antithrombotic activity, which may help improve hypercoagulability.	Red peony root: paeoniflorin (monoterpene glycoside)	Grade C

D. Detoxification and Protective Mechanisms

Overall description: reduces adverse effects of conventional treatments such as radiotherapy and chemotherapy, protects normal tissues and organ function, and improves treatment tolerance.

Table 5. Detoxification and Protective Mechanisms

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Protection of hematopoietic function (reduction of myelosuppression)	Studies suggest that its extract can increase peripheral white blood cell counts. This effect may be related to bone-marrow stimulation or immune regulation, although specific molecular targets require further study.	Eclipta: saponins (e.g., wedeloside A), wedelolactone (coumarin), flavonoids	Grade B
Protection of hematopoietic function (reduction of myelosuppression)	Its flavonoid components have antioxidant and hematopoiesis-supporting effects. Studies indicate that they may promote hematopoietic progenitor-cell colony formation, possibly through MAPK-related signaling pathways.	Spatholobus stem: flavonoids (e.g., catechins, daidzein)	Grade B
Protection of hematopoietic function (reduction of myelosuppression)	Ferulic acid may inhibit chemotherapy-induced apoptosis of hematopoietic cells, possibly through regulation of the Bcl-2/Bax protein ratio. Angelica sinensis polysaccharides may act synergistically with Astragalus polysaccharides to promote hematopoietic-factor secretion. Volatile oil components such as ligustilide may improve bone-marrow microcirculation.	Angelica sinensis: ferulic acid (phenolic acid), Angelica sinensis polysaccharides, and ligustilide (phthalides)	Grade A
Protection of hematopoietic function (reduction of myelosuppression)	Astragalus polysaccharides are major immunologically active constituents. They can activate pattern-recognition receptors such as TLR4 on macrophages and T lymphocytes, initiate intracellular signal transduction, and promote transcription and secretion of hematopoietic growth factors such as G-CSF and GM-CSF, thereby supporting hematopoiesis. Astragaloside-related saponins may also support stem/progenitor-cell proliferation and differentiation and contribute to immune-modulatory and hematopoiesis-supporting functions.	Astragalus: Astragalus polysaccharides (fructans) and astragaloside (triterpene saponin)	Grade A

Table 5 (continued). Detoxification and Protective Mechanisms

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Antioxidant and hepatoprotective effects (reduction of drug-induced liver injury)	Geniposide can promote bile secretion, possibly through increased Na ⁺ /K ⁺ -ATPase activity, thereby promoting bile flow and relieving cholestasis. Crocin has strong antioxidant activity and can scavenge free radicals.	Gardenia fruit: geniposide (iridoid glycoside), crocin (carotenoid)	Grade A
Antioxidant and hepatoprotective effects (reduction of drug-induced liver injury)	Schisandrin B is a potent activator of the Nrf2 pathway. It can interact with Keap1, promote Nrf2 dissociation and nuclear translocation, bind antioxidant response elements, and initiate transcription of phase II detoxification enzymes and antioxidant enzymes such as SOD, GST, and NQO1.	Schisandra: schisandrin B (lignan)	Grade A
Antioxidant and hepatoprotective effects (reduction of drug-induced liver injury)	Reishi/Lingzhi triterpenes have direct antioxidant and anti-inflammatory activity and may inhibit hepatic stellate-cell activation, supporting anti-fibrotic effects.	Reishi/Lingzhi: polysaccharides (β-glucans), triterpenes (e.g., ganoderic acids)	Grade B

Target/Pathway	Specific mechanism description	Related major components	Evidence level
Antioxidant and hepatoprotective effects (reduction of drug-induced liver injury)	Glycyrrhizic acid is hydrolyzed in vivo to glycyrrhetic acid. Its glucocorticoid-like structure may inhibit phospholipase A2 activity, reduce production of prostaglandins and leukotrienes, exert anti-inflammatory effects, induce heat-shock protein expression, and stabilize hepatocyte membranes.	Licorice: glycyrrhizic acid, glycyrrhetic acid (triterpene saponin)	Grade A
Improvement of overall tolerability (improved strength and function)	Rg1 may promote energy metabolism and anti-fatigue effects through activation of PI3K/Akt and CREB pathways. Rb1 has neuroprotective effects, and Rg3 may improve mitochondrial function.	Ginseng: ginsenosides (e.g., Rg1, Rb1, Rg3)	Grade A
Improvement of overall tolerability (improved strength and function)	Atractylenolides are key components for regulating gastrointestinal function; they may promote digestive-fluid secretion and enhance intestinal motility. Atractylon has anti-inflammatory activity. Together, they support spleen-stomach transformation and transportation functions.	Atractylodes macrocephala: atractylenolides (sesquiterpene lactones), atractylon (tricyclic sesquiterpene)	Grade B
Improvement of overall tolerability (improved strength and function)	Poria/Wolfiporia polysaccharides can regulate the intestinal microbiota, while triterpenes have diuretic and anti-inflammatory actions. Together, they support spleen-strengthening and dampness-draining effects.	Poria/Wolfiporia polysaccharides (pachyman), triterpenes (e.g., poricoic acids)	Grade B
Improvement of overall tolerability (improved strength and function)	Catalpol has neuroprotective, anti-inflammatory, and immunomodulatory activity. Acteoside is a strong antioxidant. Together, they may improve the systemic metabolic foundation through a yin-nourishing framework.	Rehmannia: catalpol (iridoid glycoside), acteoside (phenylethanoid glycoside)	Grade B
Improvement of overall tolerability (improved strength and function)	PSK may bind to and activate Dectin-1 and related receptors on dendritic cells, promote maturation and antigen presentation, activate T cells and NK cells, downregulate immunosuppressive TGF- β , and improve immune function.	Turkey tail polysaccharide-K (PSK, proteoglycan)	Grade A

Conclusion: Through the above multidimensional and interrelated mechanisms of action, TCMVET Baituxiao demonstrates potential roles in adjunctive canine and feline tumor therapy, including immune modulation, tumor/cancer progression management, inhibition of cancer-cell metastasis, detoxification and protective effects, induction of apoptosis, induction of cell-cycle arrest, inhibition of tumor stem cells, induction of autophagic cell death, anti-angiogenesis, inhibition of invasion and metastasis, and improvement in overall tolerability. These mechanisms are largely derived from studies of single herbs, individual components, in vitro research, and animal models, and should be interpreted by evidence tier alongside clinical evidence for the finished compound formula in dogs and cats.

IV. In Vivo Pharmacodynamics and Translational Observations of the Finished Compound Formula

4.1 Overview of the Research Evidence Chain

To supplement finished-compound-formula data beyond single-ingredient pharmacology, in vitro mechanistic research, and clinical experiential observations, the finished Baituxiao compound formula has undergone early exploratory observations in tumor-bearing mouse models and subsequent translational observations in tumor-bearing dog models. The two model types differ in research purpose, species background, tumor microenvironment, and clinical

translational value; therefore, they should not be simplistically equated but should be understood as a continuous research evidence chain.

The mouse tumor-bearing model was mainly used to evaluate preliminary effects of the finished compound formula on tumor growth dynamics, endpoint tumor weight, inflammatory factors, and histopathological changes in tumor tissue, and is considered early preclinical exploratory data. The tumor-bearing dog model more closely approximates the target animal and veterinary clinical setting, and was mainly used to observe changes in tumor burden, imaging findings, microvessel density, apoptosis, and histopathology-related indicators in canine tumor-associated models.

Given differences in study period, model design, and completeness of data, this chapter is presented according to the logic of “early exploratory observation in mouse tumor-bearing models - translational observation in tumor-bearing dog models - veterinary application interpretation.” The related results are intended to describe the *in vivo* pharmacodynamic research basis for the finished compound formula, rather than equating any single model result directly with clinical efficacy conclusions in dogs and cats.

4.2 Early Exploratory Observations in Mouse Tumor-Bearing Models

Early studies used a mouse tumor-bearing model to conduct exploratory observations on the *in vivo* pharmacodynamic trends of the finished Baituxiao compound formula. The studies mainly evaluated the effects of the finished compound formula on tumor volume, endpoint tumor weight, serum inflammatory factors, and histopathological changes in tumor tissue, with the aim of providing preliminary *in vivo* evidence for subsequent target-animal research and veterinary clinical observation.

The experimental design included a low-dose group, high-dose group, positive-control group, and blank-control group. After administration, tumor growth dynamics were observed, and tumor volume, tumor weight, serum TNF-alpha and IL-6 levels, and HE-stained tumor tissue findings were assessed at study endpoint. Tumor volume was calculated using the formula $V = 1/2 \times a \times b^2$, where a is the longest tumor diameter and b is the perpendicular shortest diameter.

The observations showed rapid tumor-volume growth in the blank-control group, whereas tumor-volume growth was relatively slower in the Baituxiao administration groups. In the high-dose group, both tumor volume and tumor weight at the observation endpoint were lower than those in the blank-control group.

Table 6. Tumor Volume and Tumor Weight Observations in an Early Mouse Tumor-Bearing Model

Group	Tumor volume on day 19 (mm ³)	Endpoint tumor weight (g)	Interpretation of observation
Low-dose group	415.0 ± 219.1	0.35 ± 0.26	Shows a certain trend toward tumor-growth inhibition
High-dose group	310.5 ± 114.4	0.27 ± 0.20	Tumor volume and tumor weight were lower than those in the blank-control group
Positive-control group	501.6 ± 188.1	0.35 ± 0.18	Serves as a similar positive reference
Blank-control group	1000.4 ± 249.0	0.79 ± 0.09	Control for natural tumor progression

4.3 Observations of Inflammatory Factors and Immune Status

In addition to tumor volume and tumor weight, early mouse tumor-bearing models also assessed serum inflammatory factors and immune-related indicators. Results showed that, compared with the blank-control group, TNF-alpha and IL-6 levels tended to decrease in the Baituxiao administration groups, suggesting that the finished compound formula may contribute to *in vivo* pharmacodynamic effects by modulating tumor-associated inflammatory responses and improving the tumor microenvironment.

TNF-alpha and IL-6 are important cytokines in tumor-associated chronic inflammation and tumor microenvironment remodeling. Abnormal elevation may be associated with tumor progression, immunosuppression, angiogenesis, and systemic wasting. These results should be regarded as supportive observations of *in vivo* immune-modulatory trends of the finished compound formula, rather than as standalone evidence for efficacy judgment.

4.4 Brief Summary of Translational Observations in Tumor-Bearing Dog Models

On the basis of early exploratory observations in mouse models, the finished Baituxiao compound formula was further evaluated through translational pharmacodynamic observations in tumor-bearing dog models. Compared with mouse models, canine models more closely approximate veterinary clinical application in body size, metabolic characteristics, immune background, and tumor biological behavior, and therefore serve as important supplementary data for evaluating the translational value of the finished compound formula in the target animal.

The tumor-bearing dog model studies used canine transplanted-tumor models, small-animal imaging, and immunohistochemistry, primarily observing tumor burden, imaging changes, microvessel density, and apoptosis-related indicators. The study data indicated supportive changes in indicators such as tumor growth-inhibition rate, reduction in microvessel density, and increased apoptotic index.

Considering differences between these studies and the early mouse models in model source, evaluation methods, and study period, this document does not directly pool data from the two model types. Instead, the tumor-bearing dog model is positioned as important supportive information bridging early preclinical exploration and target-animal translational research.

4.5 Histopathological Observations and Veterinary Interpretation

Histopathological observations showed certain differences in tumor tissues from the Baituxiao administration groups in terms of cellular density, necrotic areas, inflammatory infiltration, and tissue architecture.

Combining tumor volume, tumor weight, inflammatory factors, and imaging and immunohistochemistry-related data from tumor-bearing dog models, it can be preliminarily inferred that the *in vivo* action of the finished Baituxiao compound formula does not depend on a single target, but may be associated with multi-constituent synergistic regulation of tumor-cell proliferation, angiogenesis, inflammatory response, immune microenvironment, and apoptosis-related pathways.

From a veterinary translational perspective, mouse tumor-bearing models provide early trends in *in vivo* tumor-growth inhibition and inflammatory modulation, while tumor-bearing dog models further increase the relevance of findings to target-animal application scenarios. Together, they form a transitional evidence chain for the finished Baituxiao compound formula from constituent pharmacology and *in vivo* pharmacodynamics to veterinary clinical observation.

V. Evidence-Based Practice for Veterinary Practitioners

This guide is intended to provide veterinary practitioners with evidence-based medical information on the compound herbal preparation TCMVET Baituxiao. Based on existing *in vitro* and *in vivo* studies and clinical observational data, this product shows potential in adjunctive therapy for canine and feline tumors through multi-target mechanisms, including immune modulation, tumor/cancer progression management, toxicity reduction and efficacy enhancement, improvement in overall tolerability, and quality-of-life improvement. Evidence levels are attached to all assertions to support clinical decision-making.

Mechanism of Action: A Framework Based on Multi-Target Synergy

The advantage of this formula lies in its construction of a multidimensional, synergistic therapeutic system. It does not follow a single-action linear approach; instead, it adopts a strategy of both attack and defense, organically combining “supporting the body’s healthy qi” with “dispelling pathogenic factors.” On one hand, it systemically protects and enhances hematopoietic, immune, and vital-organ functions, improving the host’s disease resistance and treatment tolerance. On the other hand, it directly inhibits tumor-cell proliferation, promotes tumor-cell death, and blocks metastatic spread through multiple pathways. This design achieves the strategic balance of “dispelling pathogens without damaging healthy qi, and supporting healthy qi without retaining pathogens,” thereby addressing the complexity and recurrence-prone nature of tumors.

This formula deeply embodies the essence of the TCM concepts of “holism” and “treatment based on pattern differentiation.” Its intent goes beyond the local view of “treating only the site of symptoms,” focusing instead on the core pathogenesis of tumor development: the pathological environment of internal deficiency of healthy qi interbound with phlegm, stasis, and toxin. Through integrated application of therapeutic methods such as supporting healthy qi and consolidating the root, clearing heat and resolving toxicity, activating blood and transforming stasis, and softening hardness and dispersing nodules, it aims to systematically adjust the internal environment of the diseased body (that is, to change the “soil”) and fundamentally reverse the imbalanced state that favors tumor growth. This reflects the TCM principle of seeking the root in disease treatment.

From the perspective of integrative Chinese and Western medicine, its greatest value lies in the unified achievement of toxicity reduction, efficacy enhancement, and multi-target synergistic regulation. Modern pharmacological research indicates that the formula’s mechanisms encompass multiple frontier targets in contemporary tumor biology, including immune modulation, induction of apoptosis and cell-cycle arrest, inhibition of tumor angiogenesis, and reversal of drug resistance. When combined with modern veterinary treatments such as surgery and chemotherapy, it may substantially reduce toxic adverse effects from radiotherapy and chemotherapy and improve the quality of life of

affected animals. At the same time, it may modulate the tumor microenvironment, enhance the effects of mainstream therapies, and provide unique advantages for controlling tumor metastasis and recurrence, representing a more inclusive integrative-medicine pathway that places greater emphasis on quality of life.

Another potential core value of Baituxiao lies in a fundamental shift in positioning, which is also a shift for veterinary experts and pet owners: from an adjunctive role for specific diseases to a “whole-life-cycle health management plan” for middle-aged and senior dogs and cats. The core logic of this shift is that the product is no longer viewed only as a passive response to existing health problems, but as a means of proactively maintaining the health foundation of older pets through systemic support; prevention is greater than treatment. Its mechanisms form a clear closed loop: through synergistic effects of natural ingredients, it focuses on supporting immune-system function, helping manage age-related chronic inflammation, and providing foundational maintenance for key organs and cells. The ultimate goal of this multi-target synergy is to maintain internal health balance in senior dogs and cats, delay functional decline, and help pets maintain vitality and quality of life in later years.

The mechanism of action of this product (the therapeutic pathway of Baituxiao in traditional Chinese veterinary medicine theory) is based on synergistic effects following systemic absorption of multiple components. Different components act on different stages of tumor initiation and progression, generating additive and synergistic effects. The specific mechanistic pathways are shown in the figure below:

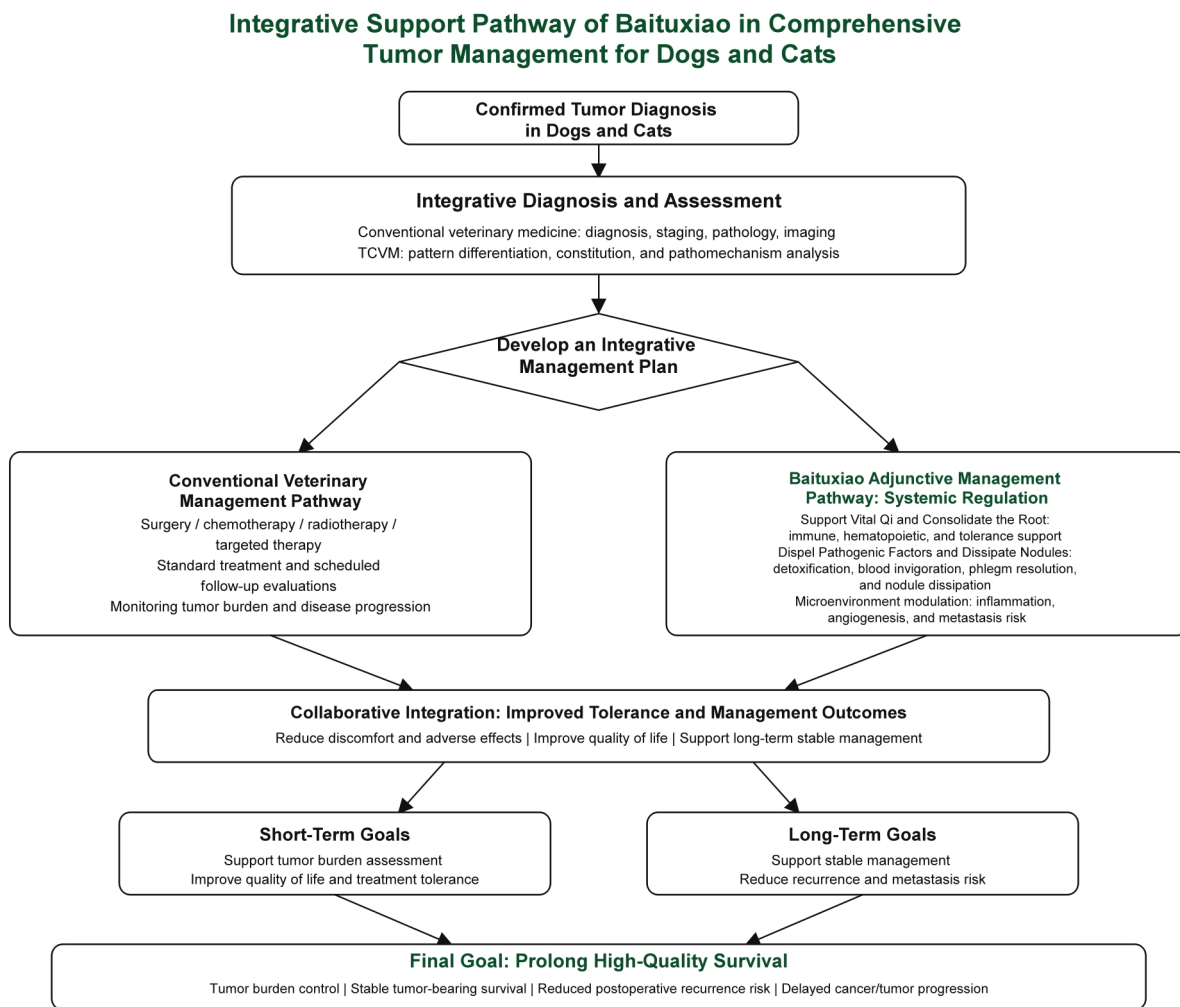


Figure 1. Integrated Support Pathway of Baituxiao in Comprehensive Tumor Management in Dogs and Cats

Pharmacological Mechanism Analysis Tables

Table 7A. Pharmacological Mechanism Analysis: Main Mechanism Table

Therapeutic dimension	Strategy	Molecular mechanism	Evidence level
Immune regulation (supporting healthy qi and consolidating the root)	Tonifies qi and secures the exterior; harmonizes ying and wei.	Regulates pattern-recognition receptor pathways such as TLR4/NF-κB.	Grade A

Therapeutic dimension	Strategy	Molecular mechanism	Evidence level
Direct antitumor support (eliminating pathogens and dispersing masses)	Detoxifies, disperses nodules, activates blood, and resolves masses.	Induces tumor-cell apoptosis/senescence, inhibits angiogenesis (VEGF), and blocks metastasis-related pathways (MMPs).	Grade A
Metabolic regulation (harmonizing yin and yang)	Transforms nutrients, raises the clear, and descends the turbid.	Regulates nutrient-sensing pathways such as AMPK/mTOR and improves insulin sensitivity.	Grade A
Organ protection (supporting healthy qi while eliminating pathogens)	Regulates the middle burner and supports free movement of qi.	Activates antioxidant pathways such as Nrf2 and regulates the activity of drug-metabolizing enzymes, including CYP450 enzymes.	Grade A
Microenvironment remodeling (pain relief and channel unblocking)	Activates blood, unblocks channels, disperses nodules, and supports analgesic comfort.	Inhibits profibrotic factors such as TGF-beta, improves tissue perfusion, and supports oxygenation.	Grade B
Anti-aging and disease-prevention support (consolidating the root and replenishing vitality)	Supports congenital vitality, resists pathogenic factors, and helps prevent disease progression.	Delays cellular senescence (e.g., through regulation of p16INK4a), maintains telomere stability, and activates autophagy.	Grade B

Table 7B. Pharmacological Mechanism Analysis: Veterinary Translational Indicators

Therapeutic dimension	Cellular/tissue effects	Animal-system effects	Veterinary clinical markers
Immune regulation (supporting healthy qi and consolidating the root)	Regulates macrophage polarization and balances lymphocyte subsets (e.g., Th1/Th2 and Treg).	Enhances resistance to common pathogens (e.g., canine parvovirus and feline calicivirus) and may support vaccine-related immune responses.	Canine: lymphocyte transformation rate, CD4+/CD8+ ratio, and serum IgG titer. Feline: response to novel antigens and nasal secretory IgA.
Direct antitumor support (eliminating pathogens and dispersing masses)	Directly inhibits tumor-cell proliferation, promotes tumor-cell death, and disrupts the tumor-supportive microenvironment.	May help control or reduce measurable solid tumors (e.g., mammary tumor and mast cell tumor) and lymphoma burden, depending on disease context and concurrent treatment.	Measurable lesions: assessed according to VCOG-RECIST / vRECIST principles using the sum of longest diameters (SLD). Circulating markers: number of circulating tumor cells (CTCs) in blood.
Metabolic regulation (harmonizing yin and yang)	Optimizes cellular energy metabolism (e.g., reduces mitochondrial dysfunction) and restores autophagy balance.	Improves overall energy level, helps maintain a healthy body-condition score (BCS), and supports normal hepatic and renal function.	Blood biochemistry: fasting blood glucose, cholesterol, triglycerides, and SDMA for renal assessment. Body-condition assessment: body weight, BCS, and muscle condition score (MCS).
Organ protection (supporting healthy qi while eliminating pathogens)	Protects hepatocytes, renal tubular epithelial cells, and intestinal mucosal cells from injury.	Reduces hepatic, renal, and gastrointestinal toxicity associated with chemotherapeutic drugs (e.g., cyclophosphamide and doxorubicin) or antibiotics.	Liver function: ALT, ALP, and total bile acids (TBA). Renal function: SDMA and creatinine (CREA). Gastrointestinal status: fecal score and frequency of vomiting or diarrhea.
Microenvironment remodeling (pain relief and channel unblocking)	Reduces stromal fibrosis and increases effector immune-cell infiltration within tumor tissue.	Improves tissue function and relieves pain or discomfort caused by tumor compression or inflammation.	Imaging: ultrasound or CT assessment of tissue perfusion and hypoxia status. Life indicators: activity level and pain score (e.g., Glasgow Composite Measure Pain Scale).
Anti-aging and disease-prevention support (consolidating the root and replenishing vitality)	Maintains stem-cell pool function, clears senescent cells, and delays tissue and organ degeneration.	Supports a healthy lifespan and helps maintain vitality, cognitive function, and muscle mass in senior dogs and cats.	Vitality indicators: 6-minute walk test and play frequency. Aging markers: relative telomere length (qPCR) and cognitive dysfunction score (e.g., CDS).

Multidimensional Research Data Analysis Table

Table 8. Multidimensional Research Data Analysis Table

Research dimension	Core finding	Key data indicators	Research methods	Evidence positioning
Computational oncology analysis	Network prediction of multi-target synergistic action	Target-coverage rate: 85-90%; network topology parameter: average degree = 12-15; pathway-enrichment significance: $p < 10^{-6}$	Network pharmacology; molecular docking; pathway-enrichment analysis	Mechanistic-prediction support data

Research dimension	Core finding	Key data indicators	Research methods	Evidence positioning
In vitro experimental validation	Significant inhibition of canine and feline tumor-cell proliferation	IC ₅₀ range: 120-400 µg/mL; apoptosis induction: 3-5-fold increase; cell-cycle arrest: G0/G1 phase 60-70%	MTT assay; flow cytometry; Western blot	In vitro mechanistic-validation data
Early exploratory mouse tumor-bearing model observation	Shows trends toward in vivo tumor-growth inhibition and cytokine regulation	Day-19 high-dose group tumor volume: 310.5 ± 114.4 mm ³ ; blank control group: 1000.4 ± 249.0 mm ³ ; high-dose endpoint tumor weight: 0.27 ± 0.20 g; blank control group: 0.79 ± 0.09 g	Mouse tumor-bearing model; tumor measurement; endpoint tumor weight; ELISA; pathological observation	Early preclinical supportive data
Tumor-bearing canine model translational observation	More closely reflects target-animal tumor burden, imaging, and pathological observation	Tumor-inhibition rate: 65-95%; microvessel-density reduction: 50-55%; apoptotic-index increase: 3-5-fold	Canine xenograft/transplant tumor model; small-animal imaging; immunohistochemistry	Target-animal translational support data
Toxicity-reduction research	Reported reduction in chemotherapy-associated toxicity indicators	White blood cell maintenance: >=4.0 x 10 ⁹ /L; ALT liver-injury marker reduction: 35-40%; improvement in body-weight loss: 60-70%	Complete blood count testing; biochemical indicator analysis; histopathology	Safety and tolerability support data
Retrospective clinical observation	Reported improvement in dogs' and cats' quality of life	Appetite-improvement rate: 80-85%; median-survival extension: 30-40%; pain-score reduction: 50-60%	Retrospective multicenter observation; survival analysis; quality-of-life scoring	Exploratory clinical observation data

Table 9. Mechanism Verification Description Table

Verification level	Verification method	Verification result	Biological significance
Molecular level	Molecular docking and surface plasmon resonance	Key components show target-binding energies < -8.0 kcal/mol	Confirms direct interaction between multiple components and core targets
Cellular level	Gene knockdown and reporter-gene assays	The observed effect is reduced by 60-70% after target knockdown	Confirms the necessity of specific signaling pathways for the observed effect
Animal level	Pathological sections and immunohistochemistry	Downregulation of phosphorylated target-protein expression in tumor tissue	In vivo validation that the proposed mechanistic pathway is biologically active

Veterinary Clinical Application Recommendations

Table 10A. Veterinary Clinical Application Recommendations: Administration Plan

Application scenario	Applicable situation	Dosage plan	Administration frequency
Adjunctive chemotherapy/radiotherapy support	Adjunctive support during tumor chemotherapy or radiotherapy	Maintenance-support frequency	Once daily at a fixed time
Adjunctive chemotherapy/radiotherapy support	Chemotherapy or radiotherapy cases with poor tolerance, weak body condition, or a need for stronger support	Enhanced-support frequency	Twice daily, once in the morning and once in the evening
Postoperative recovery support	Postoperative tumor recovery period and recurrence-risk management support	Maintenance-support frequency	Once daily at a fixed time
Postoperative recovery support	Postoperative cases with higher recovery stress, weak body condition, or a need for stronger support	Enhanced-support frequency	Twice daily, once in the morning and once in the evening
Routine support for senior or high-risk animals	Senior dogs and cats, tumor-prone animals, or long-term health management cases	Maintenance-support frequency	Once daily at a fixed time
Tumor management in affected dogs or cats	Confirmed or highly suspected tumor cases requiring long-term support or palliative management	Maintenance-support frequency	Once daily at a fixed time
Tumor management in affected dogs or cats	Cases with higher tumor burden, declining quality of life, or a need for stronger support	Enhanced-support frequency	Twice daily, once in the morning and once in the evening

Table 10B. Veterinary Clinical Application Recommendations: Course and Monitoring

Application scenario	Administration timing	Treatment-course recommendation	Monitoring indicators
Adjunctive chemotherapy/radiotherapy support	Start 5-7 days before chemotherapy or radiotherapy when feasible; administer once or twice daily according to body condition and treatment intensity.	Continue for 2-12 months after completion of treatment. Longer-term use should be determined by the veterinarian based on tumor type, follow-up findings, and tolerability.	Complete blood count, hepatic and renal function, gastrointestinal reactions, appetite, body weight, activity level, and quality-of-life score.
Postoperative recovery support	Start preoperatively or postoperatively; administer once or twice daily.	Usually continue for 2-6 months; longer-term or phased use may be considered according to follow-up results.	Wound healing, inflammatory indicators, recovery of physical strength, local recurrence or new lesions, blood biochemistry, and pain score.
Routine support for senior or high-risk animals	Once daily at a fixed time.	Long-term use may be considered, with reassessment every 3-6 months.	Vitality, body weight, appetite, muscle mass, cognitive function, blood biochemistry, and regular examination results.
Tumor management in affected dogs or cats	Administer once or twice daily. When symptoms are obvious or tumor burden is high, the veterinarian may assess whether an enhanced-support frequency is appropriate.	Long-term use may be considered, with adjustment according to clinical condition, imaging follow-up, tolerability, and quality of life.	Tumor burden, imaging changes, pain control, appetite and energy, sleep, activity, body weight, and adverse reactions.

Directions and dosage: administer orally at 1 capsule per 10 lb body weight, 1-2 times daily. For example, a 30 lb dog receives 3 capsules per dose. The actual frequency and treatment course should be determined by the veterinarian after evaluating tumor type, body condition, concurrent treatments, and tolerance.

E. Considerations for Combined Medication Use

This section describes in detail the principles for combining TCMVET Baituxiao with common drugs used in tumor treatment, with the aim of maximizing synergistic benefits and managing potential risks.

Combined Use with Chemotherapeutic Agents

Table 11. Reference for Combined Use with Chemotherapeutic Agents

Drug class	Representative drugs	Principles for combined use and potential interactions	Clinical recommendations
Antitumor antibiotics	Anthracyclines: doxorubicin, idarubicin, daunorubicin, mitoxantrone; glycopeptides: bleomycin	Synergistic efficacy support and toxicity reduction: Baituxiao may support antitumor immunity and may help reduce anthracycline-related cumulative cardiotoxicity through antioxidant and systemic-support mechanisms.	When appropriate, start Baituxiao about 1 week before chemotherapy to provide early systemic support. Monitor cardiac function.
Platinum compounds	Carboplatin, cisplatin	Synergistic sensitization and management of renal or ototoxicity: Baituxiao may provide detoxification and renal-support effects, help reduce platinum-associated nephrotoxicity or neurotoxicity, and support chemotherapy sensitivity.	Baituxiao may be used concurrently with platinum compounds or started slightly in advance, under veterinary supervision.
Alkylating agents	Cyclophosphamide, chlorambucil, lomustine (nitrosourea alkylating agent), dacarbazine (triazenoimidazole alkylating agent)	Immune modulation and reduction of myelosuppression: by supporting healthy qi and consolidating the root, Baituxiao may help maintain baseline disease resistance during periods of immune and bone-marrow suppression.	Consider continuous use before the start of a chemotherapy cycle to support the systemic foundation and help the patient pass through the myelosuppression period.
Antimetabolites	Methotrexate, cytarabine, hydroxyurea, capecitabine	May help relieve mucosal injury.	Concurrent administration may be considered, with mucosal protection as the priority.
Plant alkaloids	Vincristine, vinblastine	Baituxiao may help reduce neurotoxicity.	Continue after chemotherapy during the neurological recovery window.

Combined Use with Targeted Therapy Drugs

Table 12. Reference for Combined Use with Targeted Therapy Drugs

Drug name	Indications	Principles and potential interactions for combined use with Baituxiao	Clinical recommendations
Toceranib phosphate (Palladia®)	Canine mast cell tumor	Potentially complementary mechanisms may include tumor-angiogenesis inhibition and systemic supportive care. Separate administration may be considered to reduce gastrointestinal overlap.	Consider combined use only when the patient is clinically stable and can tolerate toceranib-associated adverse reactions such as diarrhea or vomiting. Use veterinary monitoring.
Masitinib	Canine mast cell tumor	Masitinib is metabolized mainly through hepatic CYP450 enzymes, especially CYP3A-related pathways. Because Baituxiao contains licorice and Schisandra constituents, a potential metabolic interaction should be considered, although the formula is not expected to act as a potent CYP3A4 inhibitor at routine use levels.	Use cautiously with masitinib. Avoid adding high-dose licorice or Schisandra products. Monitor for toxicity, gastrointestinal signs, liver enzymes, and clinical response; therapeutic-drug monitoring may be considered when available.
Verdinexor (Laverdia®-CA1)	Canine B-cell lymphoma	Mechanistically complementary supportive care may be considered. Main concerns with verdinexor include anorexia, vomiting, weight loss, and possible neurologic adverse effects.	Baituxiao may be administered separately, for example 1-2 hours apart, with appetite, weight, vomiting, and neurologic status monitored.
Tigilanol tiglate (Stelfonta®)	Non-metastatic mast cell tumor	Local intratumoral treatment and systemic-status support may be complementary; Baituxiao may support appetite, strength, inflammatory response, and recovery-period management.	Before and after Stelfonta® injection, combined use should be determined by the veterinarian according to local lesion response, pain, swelling, infection risk, appetite, and systemic status.

Combined Use with Biologics

Table 13A. Types of Biologics and Representative Products

Type of biologic	Drug/code	Target/platform	Indications/application scenarios
Antitumor monoclonal antibodies	Gilvetmab (gilvetmab)	PD-1	Canine mast cell tumor, melanoma, and other research or clinical exploratory scenarios
Antitumor monoclonal antibodies	P38Bf	Podoplanin (PDPN)	Canine malignant melanoma research scenario
Antitumor monoclonal antibodies	VGS-001/VGS-002	cCTLA-4/cPD-1	Canine solid-tumor combination-therapy research scenario
Antitumor monoclonal antibodies	Blontress (blontvetmab)	CD20	Canine B-cell lymphoma
Pain-management monoclonal antibodies	frunevetmab (Solensia®)	NGF	Feline osteoarthritis-related pain control
Pain-management monoclonal antibodies	bedinvetmab (Librela®)	NGF	Canine osteoarthritis-related pain control
Polyclonal antibodies / immunotherapy	Canine EGFR/HER2 peptide cancer immunotherapy	Induces anti-EGFR/HER2 polyclonal antibodies	Canine osteosarcoma and related cancer research or clinical exploratory scenarios
Therapeutic/personalized vaccine	Oncept canine melanoma vaccine	Therapeutic DNA vaccine	Canine oral or digital malignant melanoma
therapeutic/personalized vaccine	APAVAC	personalized autologous tumor vaccine	lymphoma, osteosarcoma, mast cell tumor etc. exploratory scenario
therapeutic/personalized vaccine	OST-HER2	therapeutic vaccine/bacterial vector	HER2-expressing osteosarcoma research scenario
Experimental vaccine	K9-ACV	Preventive/research vaccine platform	Multiple cancer-type research scenarios; not a conventional clinical recommendation
experimental vaccine	VACCS experimental vaccine	Hematopoiesis, immune modulation, or passive immune support	multiple cancer types research scenario; not described as a conventional clinical recommendation

Type of biologic	Drug/code	Target/platform	Indications/application scenarios
Cytokine / immune-function / blood products	EPO, G-CSF, interleukins, recombinant interferon, canine albumin, canine immunoglobulin, hyperimmune serum, etc.	hematopoiesis, immune modulation or passive immune support	anemia, leukopenia, immune-function support, or critical-care support scenarios; use must follow the original product label and veterinary judgment

Table 13B. Principles and Clinical Recommendations for Combined Use with Biologics

Type	Representative drug/platform	Principles for combined use and potential interactions	Clinical recommendations
Antitumor monoclonal antibodies	Gilvetmab, P38Bf, VGS-001/VGS-002, Blontress, etc.	Baituxiao may be considered only as adjunctive systemic-status, immune-homeostasis, appetite, strength, and quality-of-life support. It should not be claimed to replace monoclonal antibodies, enhance confirmed monoclonal-antibody efficacy, or change the prescribed antibody protocol.	The veterinarian should determine combined use and monitoring frequency according to the product label, tumor type, immune-related adverse reactions, and hematology/biochemistry results.
Pain-management monoclonal antibodies	Frunevetmab (Solensia®), bedinvetmab (Librela®)	These products are primarily used for osteoarthritis pain management rather than antitumor monoclonal-antibody therapy. Baituxiao may support overall condition, activity, and comfort in senior dogs and cats.	Monitor pain score, gait, activity, appetite, body weight, and renal/hepatic function. Do not stop or reduce the original analgesic plan solely because Baituxiao is used.
Polyclonal antibodies / EGFR-HER2 immunotherapy	Canine EGFR/HER2 peptide cancer immunotherapy	A complementary relationship may be considered from the perspective of body condition, immune homeostasis, and recovery-period management, but this remains exploratory.	Include case records, imaging follow-up, blood biochemistry, and adverse-event tracking to accumulate evidence-based data.
Therapeutic/personalized vaccine platforms	Oncept, APAVAC, OST-HER2, K9-ACV	Baituxiao may support appetite, strength, immune status, and recovery. Whether it should be paused before or after vaccination should depend on the vaccine protocol, immune status, tumor type, and veterinarian judgment.	Avoid fixed wording such as routine discontinuation for 7-15 days; individualized decisions and vaccination-response records are recommended.
Experimental vaccine platform	VACCS experimental vaccine	This is a research or exploratory platform and should not be described as a routine clinical recommendation.	Use only within research design, ethics review, or veterinary supervision; any Baituxiao combination should be recorded as exploratory supportive data.
Cytokine / immune-function / blood products	EPO, G-CSF, interleukins, recombinant interferon, canine albumin, canine immunoglobulin, hyperimmune serum, etc.	These products may be used for hematopoiesis, immune support, or critical-care support. Baituxiao should not be described as a substitute for them.	Monitor complete blood count, biochemistry, coagulation, treatment response, fever, and progression of the original disease. All use should follow the veterinary prescription and product label.

Combined Use with Analgesics (Non-Steroidal Anti-Inflammatory Drugs, NSAIDs)

General principles for NSAID combination: Baituxiao may serve as one supportive option for systemic condition, appetite, activity, and tolerance during pain management. The dose of NSAIDs, analgesics, or antitumor drugs must not be reduced independently because Baituxiao is being used concurrently. If pain, appetite, activity, or inflammatory indicators improve, the veterinarian should determine whether to adjust the original treatment plan based on pain scoring, gastrointestinal reactions, liver and kidney function, and overall condition.

Table 14. Reference for Combined Use with Analgesics (NSAIDs)

Generic drug name	Common brand-name examples	Main applicable species	Key features and precautions	Clinical recommendations
Flunixin meglumine	Banamine, etc.	Dogs: cautious/short-term use; cats: usually not recommended	Potent analgesic and anti-inflammatory NSAID; dogs require strict short-term monitoring, and feline risk is relatively high.	Monitor gastrointestinal signs, renal function, hydration status, and bleeding risk.

Generic drug name	Common brand-name examples	Main applicable species	Key features and precautions	Clinical recommendations
Mavacoxib	Trocoxil	Dogs	Long-acting NSAID mainly used for pain and inflammation related to canine degenerative joint disease.	Because of its long duration of action, monitor adverse reactions and hepatic/renal parameters carefully.
Cimicoxib	Cimalgex®	Dogs	Selective COX-2 NSAID used for canine osteoarthritis-related pain/inflammation and peri-surgical pain management.	The brand name is Cimalgex®; do not confuse it with Onsior® (robenacoxib).
Meloxicam	Metacam	Dogs and cats	Widely used NSAID; cats require feline-specific dosing and treatment plans.	Monitor appetite, vomiting, diarrhea, renal function, and hydration status.
Carprofen	Rimadyl, etc.	Dogs	Classic canine NSAID used for osteoarthritis and postoperative pain.	Monitor liver enzymes, gastrointestinal response, energy, and appetite.
Robenacoxib	Onsior®	Cats; canine use exists in some markets	Short-acting selective COX-2 NSAID; feline tablets are commonly used for short-term postoperative pain management.	Onsior® refers to robenacoxib; avoid overlap with other NSAIDs or glucocorticoids.
Firocoxib	Previcox	Dogs	Selective COX-2 inhibitor used for canine osteoarthritis and postoperative pain control.	Monitor gastrointestinal, hepatic, and renal function and avoid overlapping anti-inflammatory risk.
Grapiprant	Galliprant	Dogs	EP4 prostaglandin-receptor antagonist; non-COX-inhibiting NSAID used for canine osteoarthritis pain/inflammation.	Although the gastrointestinal, renal, and hepatic profile differs from traditional NSAIDs, use according to the label and veterinary monitoring.

Combined Use with Oncolytic Viruses

Table 15. Reference for Combined Use with Oncolytic Viruses

Species/platform	Targeted cancer type	Genetic engineering strategy and representative strain	Brief mechanism of action
Canine / vesicular stomatitis virus (VSV)	Osteosarcoma, soft tissue sarcoma, and melanoma	rVSV-DeltaM51: deletion of the M51 protein, allowing selective replication in tumor cells with deficient type I interferon signaling.	Direct oncolysis: efficient replication in cancer cells followed by tumor-cell lysis.

Table 15 (continued). Reference for Combined Use with Oncolytic Viruses

Species/platform	Targeted cancer type	Genetic engineering strategy and representative strain	Brief mechanism of action
Canine / vesicular stomatitis virus (VSV)	Osteosarcoma and other solid tumors	rVSV-IFNβ: insertion of the interferon-β gene to improve safety and strengthen antitumor immunity.	Immune activation: strong activation of innate and adaptive immunity and potential abscopal effects. Clinical research from institutions such as Mayo Clinic and the University of Minnesota suggests intratumoral administration in canine spontaneous osteosarcoma can be feasible and may induce immune-cell infiltration and systemic antitumor immunity.
Canine / vaccinia virus (VACV)	Soft tissue sarcoma, mammary tumor	TG6002: thymidine-kinase gene deletion with FCU1 insertion, enabling local conversion of a prodrug into an active chemotherapeutic agent within the tumor.	Direct viral oncolysis plus local chemotherapy; may help reverse an immunosuppressive tumor microenvironment. Veterinary clinical research in Europe has reported safety and preliminary efficacy in canine spontaneous tumors.

Species/platform	Targeted cancer type	Genetic engineering strategy and representative strain	Brief mechanism of action
Canine / reovirus	Multiple solid tumors	Reolysin (wild-type type 3 Dearing strain); enhanced replication in tumor cells with activated Ras signaling.	Selective replication and lysis in tumor cells with abnormal Ras signaling. Early exploratory canine reports and small studies suggest safety and possible synergy with radiotherapy or chemotherapy.
Canine / Newcastle disease virus (NDV)	Multiple solid tumors	Naturally attenuated strains, such as La Sota strain.	Immunogenic cell death may induce calreticulin exposure and enhance immunogenicity. Early canine exploratory research has demonstrated in vitro oncolytic activity.
Feline / Newcastle disease virus (NDV)	Lymphoma, especially FeLV-related lymphoma	Naturally attenuated strains, such as La Sota strain.	Selective replication may occur in tumor cells with deficient interferon signaling. In vitro studies suggest apoptosis induction and oncolytic potential in FeLV-positive feline lymphoma cell lines, with limited in vivo data.
Feline / feline immunodeficiency virus (FIV) vector	Lymphoma, soft tissue sarcoma	Replication-defective lentiviral vectors carrying therapeutic genes such as suicide genes or cytokine genes.	Targeted gene delivery may enable long-term expression after integration into host-cell genomes. This remains early exploratory/basic research; clinical translation is challenging because of safety and technical complexity.
Feline / feline herpesvirus (FHV-1)	Potential epithelial-origin tumors	Conceptual exploratory platform requiring targeted engineering.	Uses natural epitheliotropism, but reports are limited and engineering is difficult because FHV-1 is pathogenic in cats.
Clinical recommendation for combined use with Baituxiao	Record tumor response, immune status, adverse events, concurrent treatments, and follow-up data to support professional interpretation.		

Combined Use with Enzyme Preparations

Table 16. Reference for Combined Use with Enzyme Preparations

Species	Drug class	Representative drugs	Clinical application
Canine use	L-asparaginase	L-asparaginase (Elspar, Erwinase)	Important component of chemotherapy protocols for canine lymphoma, especially B-cell lymphoma contexts.
Canine use	Proteasome inhibitor	Bortezomib (Velcade)	Used in human multiple myeloma and mantle-cell lymphoma; veterinary use remains specialized/exploratory.
Feline use	PEG-L-asparaginase	Pegaspargase (Asparlas, Oncaspar) / L-asparaginase formulations	Exploratory or specialized use in feline lymphoma; published feline data remain limited and require oncologist supervision.

Table 16 (continued). Reference for Combined Use with Enzyme Preparations

Species	Drug class	Representative drugs	Clinical application
Feline use	PEG-L-asparaginase	Pegaspargase / L-asparaginase formulations	Reported in feline lymphoma contexts; response data should be interpreted by study design and patient selection.
Feline use	Proteasome inhibitor	Ixazomib (Ninlaro)	Mainly used in human multiple myeloma; veterinary use remains exploratory.
Commonly used in dogs and cats	Proteolytic/proteasome-related research preparations	Proteasome-related research reagents	Research use only; not a routine clinical antitumor recommendation.
Commonly used in dogs and cats	Proteasome inhibitor	MG-132 (research reagent)	Proteasome inhibitor used mainly in experimental models; not a routine clinical veterinary tumor drug.
Clinical recommendations	Document tumor type, indication, dose, monitoring plan, adverse events, and concurrent treatments.		

Combined Use with Antibiotics

Dog-Specific Antibiotics (Use with Caution in Cats)

Table 17. Reference for Combined Use with Dog-Specific Antibiotics (Use with Caution in Cats)

Antibiotic class	Representative drugs	Broad-spectrum?	Antibacterial spectrum features	Clinical application
Aminoglycosides	Gentamicin, amikacin	Yes	Strong activity against Gram-negative bacteria; some activity against selected Gram-positive bacteria.	Lower respiratory tract infection, urinary tract infection, intestinal infection
Polypeptides	Colistin sulfate	No	Strong activity against aerobic Gram-negative bacilli, including <i>Pseudomonas aeruginosa</i> .	Intestinal infection, skin infection
Fluoroquinolones	Enrofloxacin, marbofloxacin	Yes	Strong Gram-negative activity with some Gram-positive activity.	Urogenital tract infection, skin infection

Note: At present, there are no antibiotics that are exclusively for cats and completely unusable in dogs. Although amino glycosides are broad-spectrum, their use in cats is limited because of nephrotoxicity and ototoxicity. Colistin sulfate has severe nephrotoxicity and significant neurotoxicity. The renal physiology of cats makes them more sensitive to nephrotoxic drugs. Once kidney injury occurs, recovery is difficult and may progress to chronic renal failure, posing a serious threat to feline health and survival.

Veterinary-Specific Antibiotics

Table 18. Reference for Combined Use with Veterinary-Specific Antibiotics

Antibiotic class	Representative drugs	Broad-spectrum?	Antibacterial spectrum features	Clinical application
Pleuromutilins	Tiamulin, valnemulin	Yes	Activity against Gram-positive bacteria, mycoplasma, and related organisms.	Respiratory disease, mycoplasma infection
Polypeptides	Zinc bacitracin, enramycin	No	Mainly Gram-positive activity.	Intestinal infection, skin infection

Antibiotics Commonly Used in Dogs and Cats

Table 19. Reference for Combined Use with Antibiotics Commonly Used in Dogs and Cats

Antibiotic class	Representative drugs	Broad-spectrum?	Antibacterial spectrum features	Clinical application
Beta-lactams: penicillins	Amoxicillin, ampicillin	Yes	Activity against many Gram-positive and some Gram-negative bacteria; penicillinase-producing bacteria may be resistant.	Respiratory tract infection, skin and soft-tissue infection, urogenital tract infection
Beta-lactams: penicillins	Amoxicillin-clavulanate potassium	Yes	Expanded spectrum against beta-lactamase-producing bacteria because clavulanic acid inhibits beta-lactamases.	Drug-resistant bacterial infection, mixed infection, severe infection
Beta-lactams: cephalosporins	Cephalexin (first generation)	Yes	Strong Gram-positive activity with some Gram-negative activity.	Skin infection, urinary tract infection, respiratory tract infection
Beta-lactams: cephalosporins	Ceftriaxone (third generation)	Yes	Strong Gram-negative activity; long half-life; activity profile depends on organism and susceptibility.	Severe infection, meningitis, septicemia
Beta-lactams: cephalosporins	Cefixime (third generation)	Yes	Strong Gram-negative activity with some Gram-positive activity.	Respiratory tract infection, urinary tract infection
Beta-lactams: cephalosporins	Ceftiofur sodium (third generation)	Yes	Veterinary cephalosporin with activity against selected Gram-positive and Gram-negative bacteria.	Respiratory tract infection, skin infection, urinary tract infection

Antibiotic class	Representative drugs	Broad-spectrum?	Antibacterial spectrum features	Clinical application
Beta-lactams: cephalosporins	Cefovecin (third generation)	Yes	Ultra-long-acting injectable preparation; one subcutaneous injection may maintain therapeutic levels for approximately 14 days.	Canine/feline skin infection, urinary tract infection, bacterial stomatitis
Tetracyclines	Doxycycline, oxytetracycline	Yes	Activity against Gram-positive and Gram-negative bacteria, mycoplasma, chlamydia, rickettsiae, etc.	Ehrlichiosis, mycoplasma infection, respiratory tract infection
Fluoroquinolones	Enrofloxacin, ciprofloxacin	Yes	Activity against Gram-negative bacteria and selected Gram-positive organisms, chlamydia, and mycoplasma.	Intestinal infection, urinary tract infection, systemic infection
Macrolides	Azithromycin, clarithromycin	Yes	Activity against Gram-positive bacteria, mycoplasma, chlamydia, Legionella, etc.	Respiratory tract infection, skin and soft-tissue infection, mycoplasma infection
Lincosamides	Lincomycin, clindamycin	No	Mainly Gram-positive and anaerobic activity; limited Gram-negative activity.	Deep abscess, osteomyelitis, anaerobic infection
Amphenicols	Florfenicol, thiamphenicol	Yes	Broad activity against Gram-positive and Gram-negative bacteria; may also cover mycoplasma.	Respiratory disease, intestinal infection, mycoplasma infection
Sulfonamides	Sulfadiazine, co-trimoxazole	Yes	Activity against many Gram-positive and Gram-negative bacteria; may also affect chlamydia and selected protozoa.	Coccidiosis, toxoplasmosis, infection
Nitroimidazoles	Metronidazole, tinidazole	Yes	Strong activity against most obligate anaerobes and activity against selected protozoa.	Anaerobic infection, Giardia infection, oral infection

Under professional veterinary assessment and individualized medication guidance, current evidence does not indicate clear contraindicated interactions between Baituxiao and the antibiotic classes listed above. Clinical responses in affected dogs and cats should still be monitored closely during combined use.

Concurrent use of beta-lactam, fluoroquinolone, or tetracycline antibiotics with Chinese herbal medicines may carry theoretical interaction risks. These risks are mainly related to metal-ion chelation, competitive inhibition or induction of hepatic metabolic enzymes, and competition for renal excretion pathways.

When tetracycline/fluoroquinolone antibiotics are taken together with minerals that may be present in Chinese herbal medicines (such as calcium, iron, and magnesium) or botanical components rich in these elements, complexes that are difficult to absorb may form in the gastrointestinal tract, potentially reducing antibiotic bioavailability.

Many Chinese herbal components are inhibitors or inducers of hepatic cytochrome P450 (CYP450) enzymes. For example, some fluoroquinolone antibiotics are partially metabolized through CYP1A2. If an herbal formula contains components capable of inhibiting this enzyme (such as certain flavonoids), clearance of this antibiotic class may be slowed, causing accumulation, abnormally elevated blood concentrations, and increased risks of central nervous system toxicity and QT-interval prolongation.

When tetracycline/fluoroquinolone antibiotics are used together with Chinese herbal medicines (as well as other botanical or mineral supplements), staggered dosing may be used. A 2-3 hour interval is the simplest and most effective way to avoid direct interactions within the gastrointestinal tract. Staggered dosing generally does not cause problems; this simple practice is intended to ensure that both the antibiotic and our product are absorbed as completely as possible by the pet and can exert their optimal effects.

Multivalent metal ions occur naturally in plants and are distinct from excessive heavy-metal contamination. As in common foods such as spinach, nuts, and other plant materials, medicinal plants may contain naturally occurring minerals and trace elements, including calcium (Ca), magnesium (Mg), zinc (Zn), and iron (Fe). Doxycycline and enrofloxacin can transiently bind to some of these minerals in the intestine. This binding is weak and does not generate harmful substances, but it may temporarily reduce the absorption of tetracycline or fluoroquinolone antibiotics. Other antibiotic classes are generally not affected by this mechanism.

Combined Use with Hemostatic Agents

Table 20. Reference for Combined Use with Hemostatic Agents

Category	Representative drugs	Route of administration	Applicable species	Key features and mechanism of action
Injectable hemostatic drug	Etamsylate	Injection	Dogs and cats	Enhances platelet adhesion/aggregation and reduces capillary permeability; used for prevention and treatment of surgical bleeding.
Injectable hemostatic drug	Tranexamic acid	Injection	Dogs and cats	Inhibits plasminogen activation, suppresses fibrinolysis, and stabilizes clots; used for trauma or surgical bleeding.
Injectable hemostatic drug	Hemocoagulase (Reptilase/hemocoagulase)	Injection	Dogs and cats	Promotes conversion of fibrinogen to fibrin and accelerates coagulation.
Injectable hemostatic drug	Vitamin K1	Injection	Dogs and cats	Promotes hepatic synthesis of coagulation factors II, VII, IX, and X; used mainly for anticoagulant rodenticide poisoning and hepatobiliary-related coagulopathy.
Topical hemostatic drug	Epinephrine	Topical	Dogs and cats	Locally constricts blood vessels; used for emergency hemostasis of skin or mucosal bleeding.
Topical hemostatic drug	Yunnan Baiyao powder	Topical	Dogs and cats	Traditional Chinese medicine compound; may support topical hemostasis, swelling reduction, and analgesic comfort in traumatic bleeding.
Topical hemostatic drug	Absorbable gelatin sponge	Topical	Dogs and cats	Provides a physical scaffold for clot formation; used for surgical wound oozing.
Topical hemostatic drug	Chitosan hemostatic powder	Topical	Dogs and cats	Promotes platelet aggregation and activates coagulation; used for superficial wounds or nail-trimming bleeding.
Oral hemostatic drug	Carbazochrome	Oral	Dogs and cats	Enhances capillary resistance and reduces capillary bleeding; used for conditions such as epistaxis or retinal bleeding when appropriate.
Oral hemostatic drug	Yunnan Baiyao	Oral	Dogs and cats	May support hemostasis and blood-activating analgesic effects; used for internal injury bleeding or gastrointestinal bleeding under veterinary guidance.
Oral hemostatic drug	Vitamin K1	Oral	Dogs and cats	Oral dosage form used for chronic cases requiring longer-term vitamin K supplementation.

Within the current scope of understanding, there is no clear contraindication to combining Baituxiao with conventional hemostatic agents. Ingredients such as *Panax notoginseng* in the formula have traditional functions described as “stopping bleeding without retaining stasis,” and modern pharmacology supports multiple actions including promotion of coagulation, hemostasis, anti-inflammatory effects, and ulcer healing, which may help manage tumor rupture. *Panax notoginseng* can rapidly stop bleeding while also resolving blood stasis and preventing obstruction due to stasis. Its most distinctive feature is bidirectional regulation: it can stop bleeding and also activate blood and disperse stasis. Although this sounds contradictory, it is physiologically subtle. For fresh wounds, *Panax notoginseng* can rapidly promote platelet aggregation and coagulation to form a clot and stop bleeding. At the same time, saponins and other components in *Panax notoginseng* can prevent excessive clotting and thrombosis and disperse pre-existing stasis. This

is precisely the TCM concept of “stopping bleeding without retaining stasis”: stopping internal bleeding while reducing swelling and dispersing stasis.

Combined Use with Antiemetics and Appetite Modulators

During anticancer management in dogs and cats, vomiting and loss of appetite may be caused by radiotherapy, chemotherapy, anticancer drugs, adverse effects, and complications.

Table 21. Reference for Combined Use with Antiemetics and Appetite Modulators

Drug class	Representative drugs	Common brand-name examples	Main dosage forms	Key mechanism of action and clinical positioning
NK-1 receptor antagonist	Maropitant	Cerenia® (Zoetis), Emevet® (EMA)	Injection, oral tablets	Selective neurokinin-1 (NK-1) receptor antagonist; blocks substance P signaling in the central nervous system and provides broad antiemetic coverage for central and peripheral emetic stimuli, including acute and delayed chemotherapy-associated vomiting.

Table 21 (continued). Reference for Combined Use with Antiemetics and Appetite Modulators

Drug class	Representative drugs	Common brand-name examples	Main dosage forms	Key mechanism of action and clinical positioning
5-HT3 receptor antagonist	Ondansetron	Zofran®, Ondissol	Injection, oral tablets/oral solution	Blocks 5-HT3 receptors in the gastrointestinal tract and central nervous system. Particularly useful for vomiting associated with cytotoxic chemotherapy or severe inflammation, including acute chemotherapy-induced vomiting.
5-HT3 receptor antagonist	Dolasetron	Anzemet®	Injection, oral tablets	Blocks 5-HT3 receptors and may be used for nausea/vomiting related to chemotherapy or inflammatory gastrointestinal disease, according to veterinary judgment.
5-HT3 receptor antagonist	Palonosetron	No widely established veterinary brand; investigational canine palonosetron eye-drop formulations have been studied	Injection, ocular formulation	Long-acting 5-HT3 receptor antagonist with potential use for delayed chemotherapy-induced vomiting. Ocular canine formulations remain investigational/limited and should not be presented as routine standard therapy.
Multi-receptor antagonist / prokinetic	Metoclopramide	Reglan®, Maxolon	Injection, oral tablets/solution	Dopamine-antagonist and prokinetic effects; improves upper gastrointestinal motility and provides antiemetic support. It is generally weaker than NK-1 or 5-HT3 antagonists for severe chemotherapy-induced vomiting.
Phenothiazine antiemetic	Chlorpromazine	Thorazine®	Injection, oral preparation	Potent antiemetic but with higher adverse-effect risk, including sedation and hypotension; use cautiously, especially in cats.
Phenothiazine antiemetic	Prochlorperazine	Compazine®, Stemetil	Injection, oral tablets	Related to chlorpromazine; provides antiemetic and sedative effects with similar caution requirements.
Appetite stimulant / anti-nausea adjunct	Mirtazapine	Remeron®, Mirataz® (feline)	Oral tablets, transdermal ointment	Stimulates appetite and may support nausea control; Mirataz® is a feline transdermal dosage form.

Drug class	Representative drugs	Common brand-name examples	Main dosage forms	Key mechanism of action and clinical positioning
Appetite stimulant	Capromorelin	Entyce® (canine)	Oral solution	Ghrelin-receptor agonist that stimulates appetite through central hunger-regulation pathways.

When Baituxiao is used together with the above antiemetics or appetite modulators, current evidence does not identify a clear contraindication. Nevertheless, combined regimens should be individualized and monitored by a veterinarian, especially in animals with advanced disease, dehydration, anorexia, or concurrent medication use.

Combined Use with Hormonal Agents

Table 22. Reference for Combined Use with Hormonal Agents

Drug class	Representative drugs	Main dosage forms	Key clinical application	Core points and precautions
Glucocorticoids	Prednisolone	Oral tablets, injectables	Anti-inflammatory and immunosuppressive therapy; used in immune-mediated and inflammatory conditions.	Use in dogs and cats as clinically appropriate. Cats convert prednisone to prednisolone inefficiently; prednisolone is generally preferred in cats.
Glucocorticoids	Prednisone	Oral tablets, injectables	Anti-inflammatory and immunosuppressive therapy.	Requires hepatic conversion to prednisolone; conversion is reliable in dogs but limited in cats, so it is not the first choice for cats.
Glucocorticoids	Dexamethasone	Injectables, oral tablets	Potent anti-inflammatory therapy; also used in endocrine testing such as canine LDDS protocols.	Long-acting and potent; monitor gastrointestinal and systemic adverse effects, usually for short-term use.
Glucocorticoids	Budesonide	Oral preparation, inhaled formulation	Local glucocorticoid activity; oral use for intestinal inflammation/IBD contexts and inhaled use for feline asthma.	Lower systemic exposure than many systemic glucocorticoids, but adverse effects remain possible.
Glucocorticoids	Fluticasone	Inhaler	Used for feline lower-airway disease such as asthma.	Primarily local airway effect with reduced systemic exposure.
Endocrine-regulating compounds	Insulin	Injectable	Treatment of diabetes mellitus in dogs and cats.	Adjust dose according to blood glucose and clinical response; avoid hypoglycemia.
Endocrine-regulating compounds	Levothyroxine sodium	Oral tablets	Replacement therapy for canine hypothyroidism.	Requires periodic monitoring of thyroid hormone levels and dose adjustment.
Endocrine-regulating compounds	Methimazole	Oral tablets, transdermal gel	Main medical treatment for feline hyperthyroidism.	Inhibits thyroid hormone synthesis; monitor thyroid values, CBC, and liver parameters.
Endocrine-regulating compounds	Trilostane	Oral capsules	Treatment of canine hyperadrenocorticism (Cushing disease).	Inhibits adrenal steroid synthesis; requires periodic monitoring and dose adjustment.
Endocrine-regulating compounds	Desmopressin	Injection, ophthalmic/nasal preparations	Used for central diabetes insipidus and selected hemostatic indications.	Vasopressin analog; monitor hydration and sodium status where relevant.
Reproductive-related compounds	Chorionic gonadotropin	Injectable	Used in reproductive management, including ovulation-related protocols.	Use only under veterinary reproductive guidance.
Reproductive-related compounds	Pregnant mare serum gonadotropin	Injectable	Promotes follicular development in selected reproductive protocols.	May affect reproductive-cycle timing and requires specialist oversight.
Reproductive-related compounds	Mifepristone	Oral tablets	Progesterone-receptor antagonist used in selected reproductive/pregnancy-management contexts.	Use only under veterinary supervision.

Drug class	Representative drugs	Main dosage forms	Key clinical application	Core points and precautions
Immunosuppressants and targeted drugs	Cyclosporine	Oral solution, capsules	Immunosuppressive therapy for allergic/inflammatory and immune-mediated conditions.	Calcineurin inhibitor; consider drug interactions and therapeutic monitoring when indicated.
Immunomodulatory targeted drug	Oclacitinib	Oral tablets	Treatment of canine allergic dermatitis/pruritus.	JAK inhibitor with immunomodulatory effects.
Hormonal compound	Megestrol acetate	Oral tablets	Historically used for reproductive/dermatologic indications.	Adverse effects, including endocrine and mammary risks, limit routine use.
Pituitary-adrenal diagnostic compound	Adrenocorticotrophic hormone (ACTH)	Injectable	Used for adrenal function testing, including Addison disease and Cushing disease assessment.	Key diagnostic tool for canine adrenal function.
Thyroid diagnostic compound	Recombinant human thyroid-stimulating hormone	Injectable	Used for thyroid-function testing or monitoring in selected canine cases.	Stabilized TSH preparation; use according to specialist protocols.
Exploratory / special pathway compound	LOY-001	Injectable	Investigational canine longevity/senescence-delay pathway.	Mechanism is associated with IGF-1 pathway regulation; it remains an exploratory veterinary longevity product.
Calcium-regulating compound	Calcitonin	Injectable	Used for treatment of hypercalcemia and bone-metabolism disorders.	Regulates calcium metabolism; use with veterinary monitoring.

Within current veterinary understanding, no clear contraindication has been identified for combined use of Baituxiao with hormonal drugs. Under individualized guidance and continuous monitoring by a veterinary practitioner, it may have good clinical application safety.

VI. Synergy with Acupuncture Therapy

The core value of combined acupuncture and Baituxiao use lies in mechanistic complementarity and temporal synergy: acupuncture provides rapid and precise regulation of physiological function, while Baituxiao provides sustained, systemic, multi-target support. The combination can enable full-cycle management from “rapid symptom control” to “long-term functional recovery,” providing strong support for integrative treatment of tumors in dogs and cats.

Table 23. Reference for Synergistic Use of Acupuncture and Baituxiao

Treatment objective	IVAS standard acupuncture protocol	Synergy dimension	Mechanism of synergy	Clinical benefit
Immune modulation	ST36 and GV14; example needle parameters: dogs 0.25 mm × 25 mm for approximately 15 min; cats 0.16 mm × 13 mm for approximately 8 min.	Immune-function synergy	Acupuncture may activate immune cells such as NK cells and macrophages. Baituxiao contains immune-modulating constituents such as Astragalus polysaccharides and Reishi/Lingzhi polysaccharides. The combination may support cellular and systemic immune regulation within a tumor-support framework.	May support immune status during chemotherapy, reduce infection risk, and improve treatment tolerability.
Symptom control (pain/vomiting)	PC6 and related antiemetic/pain-control points; electroacupuncture may be considered when appropriate.	Metabolic and symptom-control synergy	Acupuncture can rapidly regulate neurophysiologic pathways involved in nausea/pain, while Baituxiao provides sustained multi-target inflammatory and systemic support.	May reduce cancer- or chemotherapy-associated vomiting, improve appetite, and support quality of life.
Functional recovery (postoperative/weak patients)	BL23, CV4 and related recovery-support points; parameters individualized by species and condition.	Systemic recovery synergy	Acupuncture may improve local circulation, energy metabolism, and tissue repair; Baituxiao provides systemic constitutional support and regulation.	May support wound healing, physical-strength recovery, and longer-term functional maintenance.

Notes:

For reference by certified veterinary acupuncturists.

Acupuncture procedures should be individualized according to the specific condition of the affected dog or cat. A complete assessment should be performed before acupuncture treatment to exclude contraindications. Combined treatment plans are recommended to be implemented under the guidance of an IVAS-certified veterinarian. Efficacy should be assessed regularly during treatment and the plan adjusted promptly. As an adjunctive therapy, acupuncture may help pets receiving chemotherapy maintain white blood cell levels and significantly improve appetite and energy levels. In Chinese medicine and traditional Chinese veterinary medicine, acupuncture is widely used. Clinical practice indicates that acupuncture can effectively manage tumor-related pain, chemotherapy-related adverse effects such as pain and vomiting, and improve overall quality of life in pets.

VII. Evidence-Based Synergy and Use with Botanical and Natural-Source Products

Table 24. Reference for Combined Use with Botanical and Natural-Source Products

Type	Name (Chinese/English)	Key active components	Efficacy and safety	Synergy recommendation with Baituxiao	Notes
Fungal products	Shiitake (<i>Lentinula edodes</i>)	Lentinan / shiitake polysaccharides (β -glucans)	Generally well tolerated; commonly used for immune-function support in pets.	Applicable	No special notes.
Fungal products	Chaga (<i>Inonotus obliquus</i>)	Betulinic acid, polyphenols, chaga polysaccharides, and antioxidant enzymes	Potential adjunctive tumor-support, blood-metabolism, antioxidant, anti-inflammatory, and hepatoprotective support; may irritate the gastrointestinal tract in sensitive animals.	Applicable	Use standardized products and monitor gastrointestinal tolerance.
Fungal products	<i>Cordyceps militaris</i>	Cordycepin, adenosine, cordycepic acid (D-mannitol), ergosterol, amino acids, etc.	Potential adjunctive tumor-support, immune modulation, and hepatic/renal constitutional support; excessive intake may cause soft stool.	Applicable	No special notes.

Table 24 (continued). Reference for Combined Use with Botanical and Natural-Source Products

Type	Name (Chinese/English)	Key active components	Efficacy and safety	Synergy recommendation with Baituxiao	Notes
Fungal products	<i>Cordyceps sinensis</i>	Cordycepic acid (D-mannitol), <i>Cordyceps</i> polysaccharides, amino acids, adenosine; generally low cordycepin content	May provide mild immune and constitutional support, but the tumor-adjunctive role is not clearly established.	Applicable	No special notes.
Fungal products	Reishi/Lingzhi (<i>Ganoderma lucidum</i> complex / <i>Ganoderma</i> spp.)	Reishi/Lingzhi polysaccharides, triterpenes (ganoderic acids), adenosine	Immune modulation, adjunctive tumor-support, antioxidant/anti-inflammatory effects, and hepatic/renal support. Traditionally associated with qi-tonifying and spleen-strengthening support, and may help low energy, weakness, postoperative recovery, tumor-bearing phases, and senior pets.	Not necessary	Baituxiao already contains Reishi/Lingzhi; additional use is not required.

Type	Name (Chinese/English)	Key active components	Efficacy and safety	Synergy recommendation with Baituxiao	Notes
Fungal products	Turkey tail (<i>Trametes versicolor</i> (L.) Lloyd; syn. <i>Coriolus versicolor</i>)	Turkey tail polysaccharides (PSK/PSP), glucans, phenolic compounds, sterols	Potent immune modulation, adjunctive tumor-support, hepatic/renal support, and anti-inflammatory effects. Traditionally associated with spleen-strengthening and healthy-qi support, and may help animals with low immune function, weakness, postoperative recovery, tumor-bearing phases, or chemotherapy phases.	Not necessary	Baituxiao already contains Turkey tail; additional use is not required.
Fungal products	<i>Agaricus blazei</i>	β -glucans, ergosterol, nucleic-acid derivatives, amino acids, polyphenols	Potential immune modulation and adjunctive tumor-support, including possible anti-angiogenic activity and immune-cell support; may also support appetite and inflammation control.	Applicable	No special notes.
Fungal products	<i>Phellinus linteus</i>	<i>Phellinus</i> polysaccharides, flavonoids, triterpenes, phenylpropanoids	Potential adjunctive tumor-support, especially in mammary tumor and lymphoma contexts; immune modulation, anti-inflammatory effects, and support for intestinal immune function. Vomiting, diarrhea, or skin itching may occur in sensitive pets.	Applicable	Monitor gastrointestinal and skin tolerance.
Fungal products	<i>Phellinus pini</i>	Polysaccharides, terpenoids, phenylpropanoids, flavonoids	Potential tumor-growth support, immune modulation, anti-inflammatory effects, and hepatic/renal support, especially in postoperative contexts; may cause gastrointestinal discomfort such as vomiting or soft stool.	Applicable	No special notes.
Fungal products	<i>Fomes fomentarius</i>	Organic acids, polysaccharides, flavonoids, terpenoids	Anti-inflammatory and analgesic support, adjunctive tumor-support, hepatic/renal support, and respiratory/inflammatory comfort support during tumor-bearing phases.	Applicable	No special notes.
Fungal products	<i>Shiraia bambusicola</i>	Hypocrellins and related compounds, flavonoids, polysaccharides, sterols	Potential experimental tumor-support, anti-inflammatory and analgesic effects, and respiratory comfort support; liver function should be considered before use.	Unknown	Use only with professional assessment.
Fungal products	Maitake (<i>Grifola frondosa</i>)	Maitake polysaccharides (D-fraction), β -glucans, amino acids, polyphenols	Immune modulation through macrophage and lymphocyte support, adjunctive tumor-support, and postoperative/senior recovery support.	Not necessary	Baituxiao already contains maitake; additional use is not required.

Type	Name (Chinese/English)	Key active components	Efficacy and safety	Synergy recommendation with Baituxiao	Notes
Fungal products	Poria/Wolfiporia (Wolfiporia cocos; formerly Poria cocos)	Poria/Wolfiporia polysaccharides, triterpenes (poricoic acids and related acids), sterols, amino acids	Traditionally supports spleen function and dampness metabolism; may help diarrhea tendency, appetite weakness, immune modulation, and hepatic/renal support in tumor-bearing or senior pets with weak intestinal function.	Not necessary	Baituxiao already contains Poria/Wolfiporia; additional use is not required.
Fungal products	Omphalia lapidescens	Protease-like compounds, polysaccharides, sterols	No clear core tumor-adjunctive value; traditionally used for intestinal parasites. Inappropriate use may disrupt the canine/feline intestinal microbiota and cause diarrhea or dehydration.	Not applicable	Not recommended as an adjunctive tumor-support product.
Fungal products	Puffball (Lasiosphaera seu Calvatia)	Ergosterol derivatives, puffball-related compounds, organic acids, amino acids, adhesive proteins	Traditionally used for throat discomfort and hemostasis; may be relevant to throat irritation, hoarseness, cough, epistaxis, or traumatic bleeding, but tumor-adjunctive evidence is limited.	Not applicable	No special notes.

Table 24 (continued). Reference for Combined Use with Botanical and Natural-Source Products

Type	Name (Chinese/English)	Key active components	Efficacy and safety	Synergy recommendation with Baituxiao	Notes
Fungal products	Polyporus umbellatus	Polyporus polysaccharides, sterols, triterpenes	Supports water metabolism and dampness drainage; may serve as adjunctive body-condition management for tumor-bearing or senior pets. Use in dogs/cats with impaired hepatic or renal function or dehydration risk requires veterinary assessment; excessive intake may cause soft stool or diarrhea.	Use with caution	Monitor hepatic/renal function, hydration, water intake, dosage, and dehydration risk.
Fungal products	Armillaria mellea	Armillaria polysaccharides, ergosterol, adenosine, neuromodulatory amide compounds	May support neurologic function, antioxidant status, and senior-pet recovery; no clear tumor-adjunctive role is established.	Unknown	No special notes.
Fungal products	Marasmiellus androsaceus	Polysaccharides, ergosterol, flavonoids, terpenoids	Traditionally used to dispel wind and unblock collaterals; may provide anti-inflammatory, analgesic, and mobility comfort support for inflammatory, neurologic, or senior-phase discomfort.	Unknown	No special notes.

Type	Name (Chinese/English)	Key active components	Efficacy and safety	Synergy recommendation with Baituxiao	Notes
Fungal products	Laetiporus sulphureus	Polysaccharides, flavonoids, terpenoids, polyphenols	Potential immune modulation, adjunctive tumor-support, inhibition of tumor-cell proliferation, anti-inflammatory effects, and hepatic/renal support; may be considered during tumor-bearing or inflammatory phases.	Unknown	Use only with professional assessment.
Fungal products	Claviceps purpurea	Ergot alkaloids, including ergocornine and related compounds	High-risk in dogs and cats. Ergot alkaloids can cause vasoconstriction, muscle spasms, vomiting, diarrhea, convulsions, sudden blood-pressure elevation, and potentially multi-organ failure. No safe dosage is established for companion-animal supportive use.	Contraindicated	Do not use.
Fungal products	Cordyceps cicadae	Cordyceps cicadae polysaccharides, cordycepic acid (D-mannitol), adenosine, ergosterol, amino-acid compounds	Potential immune modulation, adjunctive tumor-support through immune and cellular activity, hepatic/renal support, and respiratory comfort support such as cough or wheezing relief.	Applicable	No special notes.
Fungal products	Dictyophora indusiata	Dictyophora polysaccharides, multiple amino acids, trace elements such as zinc and selenium, and other compounds	Immune modulation, antioxidant support, tumor-adjunctive support, and respiratory comfort support.	Applicable	No special notes.
Fungal products	Morchella esculenta	Morchella polysaccharides, ergosterol, essential amino acids, trace elements such as selenium, zinc, iron, and B vitamins	Immune modulation through macrophage/cellular activity, high-protein low-fat nutritional support, postoperative recovery support, antioxidant and metabolic characteristicsupport for tumor-bearing, senior, weak, or postoperative pets.	Applicable	No special notes.
Herbal products	Echinacea	Alkylamides, inulin	Generally safe for short-term immune support.	Applicable	Short-term use only (for example, up to 6 weeks unless otherwise directed).
Herbal products	Milk thistle	Silymarin / silybin	Generally safe; a standard hepatoprotective-support ingredient for dogs and cats.	Applicable	Use standardized silymarin/silybin products; long-term use is generally well tolerated.
Herbal products	Slippery elm bark	Mucilage	Generally safe; acts as a gastrointestinal mucosal protective agent.	Applicable	Give separately from Baituxiao and other medications, ideally by at least 1 hour.
Herbal products	Ginkgo biloba	Ginkgo flavonoids and terpene lactones	Use cautiously because of possible effects on coagulation and bleeding risk, especially during the perioperative period or when anticoagulant/antiplatelet drugs are used.	Contraindicated / generally not recommended	Risk may exceed benefit in many tumor-care scenarios.

Type	Name (Chinese/English)	Key active components	Efficacy and safety	Synergy recommendation with Baituxiao	Notes
Herbal products	Turmeric	Curcuminoids	Generally safe at appropriate doses; bioavailability is low and may be improved by formulation strategies. May irritate the gastrointestinal tract in some animals.	Applicable	Use after feeding and monitor gastrointestinal tolerance.
Herbal products	St. John's wort	Hypericin, hyperforin and related compounds	Potent hepatic enzyme inducer; may significantly reduce exposure to Baituxiao-associated constituents and multiple chemotherapy or supportive drugs.	Contraindicated	Avoid combined use with Baituxiao and multi-drug treatment regimens.
Herbal products	Bloodroot	Sanguinarine and related alkaloids	High toxicity risk. Oral or inappropriate topical use may cause severe tissue necrosis and systemic organ injury.	Contraindicated	Do not use orally.

Table 24 (continued). Reference for Combined Use with Botanical and Natural-Source Products

Type	Name (Chinese/English)	Key active components	Efficacy and safety	Synergy recommendation with Baituxiao	Notes
Herbal products	Sage	Thujone, camphor and related volatile oils	High doses may carry neurotoxicity risk; dosage and duration must be strictly controlled.	Use with caution	Use low doses and short courses only.
Herbal products	Rosemary	Carnosic acid, rosmarinic acid	Generally safe as an antioxidant and preservative-support ingredient when standardized and appropriately dosed.	Applicable	Use standardized extracts and avoid excessive concentration.
Herbal products	Lemon balm	Terpenes, aldehydes, polyphenols	Generally safe; may provide calming, anti-inflammatory, and antioxidant support.	Applicable	Generally safe; monitor for excessive sedation.
Herbal products	Basil	Aromatic volatile compounds	Generally safe in culinary-level amounts; may provide anti-inflammatory, analgesic, and digestive support.	Applicable	Use as supportive anti-inflammatory/nutritional support only.
Herbal products	Rhodiola	Rosavins, salidroside and related compounds	Generally safe at appropriate doses; may help stress resilience and fatigue.	Applicable	May be better used earlier in the day.
Herbal products	Marshmallow root	Mucilage	Generally safe; provides mucosal protection, water-metabolism support, anti-inflammatory comfort, and swelling-related support.	Applicable	Separate from other medications by about 2 hours.
Herbal products	Stinging nettle	Flavonoids, phytosterols	Generally safe; may support skin itching and inflammatory comfort.	Applicable	Supportive use only.
Herbal products	Calendula	Flavonoids, triterpene saponins	Generally safe; oral or topical use may support skin comfort, anti-inflammatory effects, and immune regulation.	Applicable	Generally safe when appropriately prepared.

Type	Name (Chinese/English)	Key active components	Efficacy and safety	Synergy recommendation with Baituxiao	Notes
Herbal products	Olive leaf	Oleuropein and polyphenols	Generally safe; antioxidant and immune-supportive effects.	Applicable	Broad-spectrum supportive use.
Fruit/berry products	Elderberry	Anthocyanins; cyanogenic glycosides may be present in some plant parts	Use with caution. Leaves, stems, and unripe parts may contain cyanogenic glycosides; use only standardized pet-appropriate preparations.	Use with caution	Use professionally formulated extracts only.
Fruit/berry products	Blueberry	Anthocyanins	Generally safe; antioxidant, intestinal, and protective support.	Applicable	Fresh or dried pet-appropriate forms may be used.
Fruit/berry products	Sea buckthorn	Vitamin C, vitamin E, carotenoids	Generally safe; protective support for skin and mucosa.	Applicable	Supportive use.
Fruit/berry products	Goji berry	Goji polysaccharides	Generally safe; hepatic/renal support, immune support, and protective effects.	Applicable	Use in appropriate amounts.
Extracts/oils	CBD (cannabidiol)	Cannabidiol	Relative safety depends on dose and product quality. May affect hepatic enzymes; THC content must be carefully controlled and should comply with local regulations.	Applicable with veterinary oversight	Use low doses, monitor liver enzymes, and avoid THC-containing products.
Extracts/oils	Hemp oil	Omega fatty acids	Generally safe; not equivalent to CBD/THC and mainly serves as nutritional fatty-acid support.	Applicable	Long-term nutritional support.
Extracts/oils	Grape seed extract	Proanthocyanidins (OPCs)	Generally safe at appropriate extract doses; distinct from grapes/raisins and should be used as a standardized extract.	Applicable	Control dosage.
Extracts/oils	Pine needle extract	Proanthocyanidins, terpenes	Plant material can be problematic depending on species; only clearly identified, safe, standardized extracts should be considered.	Use with caution	Use only verified safe species and standardized extracts.
Other	Aloe vera	Aloe polysaccharides; anthraquinone compounds in latex-containing preparations	Use cautiously for oral administration. Latex-type components may cause vomiting, diarrhea, or bloody diarrhea; oral products must be purified and pet-appropriate. Topical use is relatively safer.	Use with caution (oral use)	Avoid household aloe products for oral use unless purified and professionally formulated.
Other	Catnip	Nepetalactone and related volatile compounds	Generally safe for cats and may have behavioral/calming effects. In dogs, it may cause gastrointestinal discomfort and has limited supportive value.	Feline only / use with caution	Use mainly in cats; avoid routine canine use.
Other	Parsley	Apigenin, volatile oils	Generally safe in small amounts; vitamin K content and medication context should be considered.	Applicable	Use as flavor/nutritional support, not as treatment-dose therapy.

Type	Name (Chinese/English)	Key active components	Efficacy and safety	Synergy recommendation with Baituxiao	Notes
Other	Beetroot	Betalains and organic acids	Generally safe; may change stool or urine color and should not be mistaken for bleeding without assessment.	Applicable	Use in appropriate amounts.
Other	Yucca	Saponins	May carry toxicity risk in dogs. Saponins can cause vomiting, diarrhea, and potentially hemolytic effects at higher exposure. Feline safety data are limited.	Not recommended, especially in dogs	Avoid routine use in canine and feline tumor-support protocols.

Notes:

Applicable: mechanisms are complementary, no known serious interactions, and combined use can be considered safe.

Use with caution: potential synergy exists, but dose, specific risks, or individual variation require close monitoring.

Contraindicated: high-risk interactions exist; combined use is prohibited.

Unknown: interactions after combined use cannot be clearly determined, including synergistic/antagonistic effects and safety risks.

Not applicable: overlapping ingredients or other circumstances make combined use unsuitable.

Species specificity: some ingredients are species-specific. Catnip is safe and effective only for cats and is not recommended for dogs.

VIII. Safety and Monitoring

Safety: Based on clinical application data and long-term pet feeding validation, Baituxiao uses a scientifically balanced combination of natural medicinal fungi and herbal ingredients. When the recommended dosage is followed, available application and feeding-tolerance data support a favorable safety profile, with good tolerability and a low observed risk in dogs and cats.

Monitoring recommendations: observe appetite, mental status, and stool form to intuitively assess adaptation. Routine complete blood count and serum biochemistry testing are recommended every 1-2 months, with attention to liver and kidney function indicators. The veterinarian should evaluate tolerance, clinical response, and monitoring data, and adjust the use plan accordingly.

IX. Efficacy Assessment and Follow-up

Core Assessment Principles

These assessment standards are intended to document and evaluate the contribution of Baituxiao across multiple objectives. Assessment should run throughout treatment and use a multidimensional approach combining quantitative and qualitative methods.

Efficacy assessment standards (short-term: 1-3 months after treatment initiation). The following indicators should be recorded before treatment (baseline) and regularly during treatment to assess short-term effects.

Table 25A. Efficacy Assessment Standards: Short-Term Assessment Indicators

Assessment dimension	Specific indicators and assessment tools	Assessment frequency	Relationship to Baituxiao mechanisms
Tumor response (clinical objective)	Lesion measurement according to RECIST/VCOG-RECIST concepts or relevant disease-specific standards. Use caliper measurement or imaging (ultrasound, radiography, CT) where appropriate. For lymphoma and other hematologic tumors, use appropriate staging and response criteria rather than simple mass measurement.	Every 4-8 weeks	Direct antitumor-support pathways, including apoptosis induction and proliferation inhibition.

Assessment dimension	Specific indicators and assessment tools	Assessment frequency	Relationship to Baituxiao mechanisms
Quality of life (client-reported and clinical)	Quality-of-life score using tools such as HHHHHMM or COHS; assess pain, appetite, activity/energy, and adverse effects such as vomiting or diarrhea.	At each recheck, e.g., every 2-4 weeks	Organ-protection and immune-modulation pathways; toxicity reduction and overall-status support.
Laboratory indicators (client safety / monitoring)	CBC: focus on leukocytes, neutrophils, platelets, and anemia to assess bone-marrow support. Serum biochemistry: monitor ALT, ALP, creatinine, BUN, and related indicators for hepatic/renal safety. Inflammation markers such as CRP may be considered to assess systemic inflammation.	Concurrent with chemotherapy or every 4 weeks	Organ-protection and immune-modulation pathways, including hematopoietic protection and hepatic/renal risk reduction.
Treatment tolerability	Chemotherapy completion rate, dose-intensity maintenance, treatment delays, dose reductions, appetite, vomiting, diarrhea, body weight, and owner-reported tolerance.	After each chemotherapy cycle	Core value: overall tolerability and sustained treatment participation.

Table 25A (continued). Efficacy Assessment Standards: Short-Term Assessment Indicators

Assessment dimension	Specific indicators and assessment tools	Assessment frequency	Relationship to Baituxiao mechanisms
Adverse-event grading	Record and grade adverse events according to VCOG-CTCAE terminology where applicable, including gastrointestinal, hepatic, renal, hematologic, and behavioral signs.	At each recheck and whenever clinical signs occur	Safety monitoring and tolerability assessment during integrated tumor management.

C. Long-Term Follow-up Indicators (medium to long term: after 3 months of treatment and after treatment completion)

Table 25B. Long-Term Follow-up Indicators

Follow-up objective	Core indicator	Follow-up time point	Significance
Progression-free survival (PFS)	Time from treatment initiation to tumor progression or recurrence.	Every 2-3 months after treatment completion	Assesses duration of disease control and provides a direct clinical indicator of adjunctive support.
Overall survival (OS)	Time from treatment initiation to death from any cause or defined endpoint.	Continue follow-up until endpoint	Assesses overall clinical benefit; interpretation must consider tumor type and concurrent treatment.
Long-term quality of life	Continue quality-of-life scoring; focus on muscle condition, cognitive function in senior dogs/cats, activity, appetite, and comfort.	Every 1-3 months after treatment completion	Assesses the role of Baituxiao in maintaining long-term quality of life.
Late toxicity	Continuous monitoring of hepatic/renal function and organ function, especially if anthracycline or other organ-toxic drugs are used.	Every 3-6 months after treatment completion	Assesses long-term safety.

This assessment system translates the multi-target mechanisms of Baituxiao into quantifiable and trackable clinical indicators, enabling veterinarians to:

Objectively evaluate its value in adjunctive therapy; document concrete follow-up changes for pet owners, such as smaller measured lesions or improved energy and appetite; and lay the foundation for accumulating higher-level clinical evidence. We recommend that veterinarians actively apply these standards in clinical practice, and we welcome feedback data to jointly improve standards for adjunctive treatment of pet tumors.

X. Exploratory Clinical Observations and Real-World Case Data

10.1 Evidence Positioning

This chapter supplements exploratory clinical observations and real-world case data for Baituxiao in integrated tumor management in dogs and cats. The value of this information lies in presenting actual-use scenarios, owner observations,

imaging or functional changes, and safety feedback. Its limitations are that most cases still lack standardized case report forms, blinded assessment, placebo controls, complete pathological classification, and long-term follow-up. Therefore, this chapter is not presented as confirmatory efficacy conclusions, but as a reference for future veterinary clinical research design and case-database development.

10.2 Exploratory Clinical Observations in China

Existing data from China have accumulated feedback from thousands of canine and feline tumor-related uses, covering scenarios such as postoperative adjunctive management, conservative observation of benign masses, long-term tumor-bearing management, and quality-of-life support. This guide does not include all cases individually in the main text; instead, it selects representative de-identified cases from existing data as references and positions them as exploratory clinical observational data. Because this information still has limitations such as tumor-type heterogeneity, incomplete pathological confirmation, differences in concurrent treatment, and variation in follow-up duration, the related results should be interpreted together with standardized case report forms, imaging data, pathological or cytological results, and veterinary assessment.

De-identified Chinese case 1: postoperative adjunctive management. A canine postoperative tumor case used Baituxiao as an adjunctive support plan on the basis of routine postoperative management. Records indicated that during the observation period, the owner reported relatively stable energy, appetite, and activity, and no obvious adverse reactions were observed during postoperative rechecks. This case is suitable for inclusion in the “postoperative recovery and recheck observation” scenario. Future supplementation should include pathological subtype, margin status, staging results, concurrent medications, and serial imaging data.

De-identified Chinese case 2: conservative observation of a benign mass. A senior dog/cat mass case did not immediately undergo surgery because of age, anesthesia risk, owner preference, or other factors, and Baituxiao was used for conservative observation on the basis of regular rechecks and quality-of-life management. Records focused on mass size, texture changes, energy and appetite, body weight, and activity. The value of this type of case lies in presenting long-term management scenarios for elderly animals or animals with higher anesthesia risk, and efficacy should not be judged solely by a single change in mass size.

De-identified Chinese case 3: long-term tumor-bearing management. A dog/cat case with a confirmed or highly suspected tumor underwent long-term supportive management while remaining tumor-bearing. Owner observations focused on pain, appetite, activity, body weight, sleep, and daily comfort. This type of case is suitable for establishing an observational framework for quality of life and palliative management. Future addition of complete blood count, biochemical, imaging rechecks, pain scores, and veterinarian-signed confirmation would further improve research value.

Table 26. Dimensions of Exploratory Clinical Observation Data

Observation dimension	Data that may be included	Veterinary interpretation focus
Postoperative adjunctive management	Postoperative wound/local status, recovery, physical strength, appetite	Supports postoperative recovery-period observation and management.
Conservative observation scenario	Mass size, imaging changes, quality of life, whether surgery/anesthesia was deferred	Useful for elderly animals or cases with relatively high anesthesia risk.
Tumor-bearing management	Pain, appetite, activity, body weight, stability of daily comfort	Focuses on symptom burden, quality of life, and tumor-related changes.
Safety	Complete blood count, biochemistry, gastrointestinal reactions, adverse events	Requires standardized adverse-event recording.

10.3 Selected Real-World Cases from Europe and North America

During 2025-2026, real-world feedback from thousands of canine tumor uses was accumulated in regions including the United States, the United Kingdom, the Netherlands, Poland, and Belgium. To avoid overinterpretation from case accumulation, this guide selects only some representative cases with relatively complete information that reflect different application scenarios, and presents them uniformly as “case observations.”

Case 1: canine liver tumor case from Poland. In a canine liver tumor case from Poland, the owner reported that after approximately 3 consecutive months of Baituxiao capsule use, follow-up ultrasound showed that one liver tumor lesion had decreased in size compared with prior imaging. The dog’s overall condition was good, and repeat purchase was completed. The value of this case lies in the simultaneous presence of treatment duration, imaging recheck, lesion change, life-status feedback, and repurchase behavior. It is recommended that future documentation include pre- and

post-use ultrasound reports, tumor measurement values, liver-function indicators, body-weight changes, whether other drugs were used concurrently, and veterinary diagnostic records to improve evidence level.

Case 2: postoperative management of a canine splenic tumor in the United Kingdom. In a UK canine high-risk splenic tumor case, Baituxiao capsules were used as a postoperative adjunctive management plan after surgery. The original data described imaging rechecks after several months of continued use; the owner reported good body weight, mental status, and daily activity, and imaging follow-up showed no obvious abnormality. This case is suitable for positioning as a “postoperative adjunctive management and follow-up observation” case, rather than being directly described as confirmatory complete remission. Future documentation should include pathological type, margin status, staging results, whether chemotherapy was used concurrently, and original imaging reports.

Case 3: improved urination function in a canine bladder tumor case in the United States. In a US canine bladder tumor case, the owner reported that the dog had experienced marked difficulty urinating and could only dribble urine. After several months of continuous Baituxiao capsule use, the owner observed improved urination status, more stable urine flow, and improved quality of life. The core value of this case lies in functional endpoints and comfort improvement, making it especially suitable for inclusion in palliative management and quality-of-life support scenarios. Future documentation should include bladder ultrasound, urinalysis, urine culture, cytology or histopathology, and exclusion of confounders such as infection, stones, inflammation, analgesics, or antibiotics.

Case 4: comfort improvement in a canine oral tumor case in the Netherlands. In a Netherlands canine oral tumor case, the owner reported oral bleeding, frequent pawing at the mouth, and breathing discomfort. After Baituxiao capsule use, the owner observed reduced oral discomfort, less bleeding, and improved respiratory status. This case is suitable for inclusion in the “comfort support and quality-of-life improvement” category. Future documentation should include oral examination, imaging or endoscopic data, cytology or pathology results, bleeding and pain scores, and records of concurrent analgesic or anti-infective treatment to improve evaluability of the case data.

10.4 Recommendations for Case-Data Standardization

To upgrade ordinary customer feedback into real-world evidence that can be evaluated by veterinarians, a standardized case report form (CRF) is recommended. Each case should record at minimum: country, year, breed, age, sex, body weight, tumor type, diagnostic method, pathological or cytological results, staging results, pre-use imaging, post-use imaging, tumor measurement data, Baituxiao dose and duration, concurrent treatments, changes in appetite and energy, pain scores, mobility, complete blood count, biochemical, adverse events, owner authorization, and veterinarian-signed confirmation.

Table 27. Recommendations for Standardizing Real-World Case Data

Data category	Required contents	Purpose
Diagnostic data	Pathology/cytology, staging, measurable lesions	Confirm case type and allow evaluability.
Use data	Dosage, frequency, course duration, concurrent treatments	Assess exposure, confounders, and safety.
Tumor / management indicators	Tumor size, pain, appetite, activity, body weight, activity level	Enable multidimensional assessment.
Safety data	Complete blood count, biochemistry, coagulation, gastrointestinal reactions, adverse events	Support long-term risk assessment.
Authorization text	Owner authorization, veterinarian confirmation, data-use permission	Increase traceability and professional credibility.

10.5 Summary

At present, real-world data suitable for inclusion in the main text of the guide should primarily consist of a small number of high-value cases, avoiding overinterpretation of case observations as general efficacy. If complete CRFs, imaging data, pathology reports, and veterinary confirmation can be added in the future, this section will more closely approximate high-quality real-world research data.

XI. Abbreviations

The following abbreviation table is used to standardize English abbreviations and their meanings in this guide, allowing veterinarians to quickly consult terms while reading the mechanisms, monitoring, and clinical assessment sections.

Table 28. Abbreviations

Abbreviation	Full English name	Explanation
ALT	Alanine aminotransferase	Hepatocellular monitoring indicator
ALP	Alkaline phosphatase	Indicator related to cholestasis, hepatobiliary disease, and bone activity
AMPK	AMP-activated protein kinase	Energy-sensing kinase related to metabolic regulation and autophagy
BCS	Body condition score	Body-condition assessment score
BUN	Blood urea nitrogen	Indicator related to renal function and protein metabolism
caspase	Cysteine-aspartic protease	Core enzyme family in the apoptosis cascade
CD4+/CD8+	T-lymphocyte subset ratio	Indicator of T-cell subset balance and immune status
COHS	Canine Owner-Reported Health Status	Owner-reported canine health-status assessment tool

Table 28 (continued). Abbreviations

Abbreviation	Full English name	Explanation
CRP	C-reactive protein	Systemic inflammation indicator
CT	Computed tomography	Cross-sectional imaging modality
CTCAE	Common Terminology Criteria for Adverse Events	Standard terminology for adverse-event grading; veterinary adaptation includes VCOG-CTCAE
CYP450	Cytochrome P450	Drug-metabolizing enzyme system
DC	Dendritic cell	Antigen-presenting immune cell
EMT	Epithelial-mesenchymal transition	Process related to invasion and metastasis
HIF-1 α	Hypoxia-inducible factor 1-alpha	Hypoxia-responsive factor related to VEGF and angiogenesis
IC ₅₀	Half-maximal inhibitory concentration	In vitro potency indicator
IFN- γ	Interferon gamma	Th1 and antitumor immune-related cytokine
IL	Interleukin	Cytokine family
MCS	Muscle condition score	Muscle-condition assessment score
MMP	Matrix metalloproteinase	Enzyme family related to extracellular-matrix degradation and invasion
NF- κ B	Nuclear factor kappa-light-chain-enhancer of activated B cells	Core transcription factor in inflammation and immune signaling
NK	Natural killer cell	Innate immune effector cell
NSAIDs	Non-steroidal anti-inflammatory drugs	Anti-inflammatory and analgesic drug class
OS	Overall survival	Overall survival endpoint
PFS	Progression-free survival	Time without progression endpoint
PI3K/Akt	Phosphoinositide 3-kinase/protein kinase B pathway	Signaling pathway related to cell survival, proliferation, and metabolism
PSK	Polysaccharide-K	Protein-bound polysaccharide from Turkey tail
PSP	Polysaccharopeptide	Protein-bound polysaccharopeptide from Turkey tail
SDMA	Symmetric dimethylarginine	Early renal-function monitoring indicator
TGF- β	Transforming growth factor beta	Immunosuppressive and EMT-related cytokine
TLR4	Toll-like receptor 4	Innate immune pattern-recognition receptor
TME	Tumor microenvironment	Tumor-associated cellular and stromal microenvironment
TNF- α	Tumor necrosis factor alpha	Inflammatory cytokine
VEGF	Vascular endothelial growth factor	Core angiogenesis factor
VEGFR	Vascular endothelial growth factor receptor	VEGF receptor family

XII. Evidence Sources and References

A. Principles for Citing Evidence Sources

Evidence sources in this guide are divided into three categories. The first includes canine and feline clinical studies, veterinary oncology consensus documents, and official drug information. The second includes in vitro and animal studies of constituent herbs or extracts. The third includes human oncology, pharmacokinetic, or safety studies. Research at the constituent or medicinal-material level can support mechanistic plausibility, but should not automatically be equated with confirmatory clinical efficacy of the finished compound formula in dogs and cats. The finished compound formula still requires further validation through its own prospective studies, retrospective case cohorts, or real-world data.

B. Methodology and Limitations Statement

This version is an academic guide and application reference document. Literature supplementation primarily draws on veterinary oncology consensus documents, canine and feline clinical studies, official drug information, constituent pharmacology studies, and related safety research to support mechanistic, monitoring, and safety discussions. Because prospective controlled studies and real-world case data for the finished formula in dogs and cats still require further supplementation, this document interprets constituent evidence, medicinal-extract evidence, compound-theory evidence, and finished-product clinical evidence by evidence tier. For specific diagnosis, staging, combined medication use, and efficacy judgment, the examination and assessment of the individual animal by a licensed veterinarian should remain the basis.

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Appendix: Charitable Assistance

We have always believed that the growth of an enterprise is inseparable from giving back to society. Over the years, we have continued to support stray-animal rescue efforts and have been committed to contributing what we can. To put this support into practice, we provide free product assistance to legally registered stray-animal rescue bases/institutions. To ensure that resources are delivered accurately, please provide official registration certificates and daily rescue records for review. We are willing to work with you to protect the health of pets.

Support plan for individual rescuers: In the past, we have provided some Baituxiao free of charge to individual rescuers. “We deeply understand that countless compassionate individual rescuers are the most direct angels for stray animals. TCMVET Baituxiao is willing to support you. To ensure that resources accurately help the small lives that truly need them, we have established a simple verification process. If you have been providing long-term rescue and are facing difficulties, please contact us. We will do our best to provide assistance according to the actual situation.”

Conclusion:

Comprehensive cancer management extends beyond a purely technical domain; it is a journey requiring close cooperation between pet owners and the veterinary team. This guide systematically outlines an evidence-based approach intended to support that journey: helping pet owners better understand the treatment process and become active participants, while providing veterinarians with additional clinical tools and enriching their treatment decision options. Future clinical practice and research will further validate and optimize these approaches.

Academic support: Hong Kong Pet Tumor Research Association

Guide links: www.tcm-vet.com/baituxiao-guidelines; www.baituxiao.com/baituxiao-guidelines; www.dogtumor.com/baituxiao-guidelines

About Us:

We are committed to the research and development of advanced pet supplements. We provide high-quality pet supplements; high quality is our baseline, and we do not compromise quality to reduce costs. Pet health issues are complex and diverse. Both modern veterinary medicine and Chinese medicine approaches may encounter different levels of challenge when facing complex chronic problems.

Official websites: www.tcm-vet.com; www.baituxiao.com

Contact us: info@tcm-vet.com; info@baituxiao.com

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All information contained in this document, “Academic Guide and Application Reference for TCMVET Baituxiao in Integrated Tumor Management in Dogs and Cats,” including but not limited to text, charts, and recommended plans, is for educational and reference purposes only and does not constitute medical advice or a prescription. All diagnosis and treatment decisions must be made by a licensed veterinarian after a comprehensive examination of the individual animal. The publisher and authors assume no legal responsibility for any direct or indirect consequences arising from the use, misuse, or reliance on information contained in this document. Product information may be updated; please refer to the latest official documents.

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