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Herbal Approaches in Canine Mammary Tumor Therapy

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INTRODUCTION

Canine mammary tumors (CMTs) represent 42–52% of all tumors in intact female dogs and remain a leading cause of neoplastic mortality in companion animals (Sorenmo et al., 2020). Their pathogenesis is multifactorial, involving hormonal, genetic, and environmental influences. Among the most significant risk factors are prolonged exposure to estrogen and progesterone, delayed ovariohysterectomy, obesity, and high-fat dietary intake, all of which contribute to tumor initiation and progression. The incidence of mammary neoplasia can be reduced by up to 90% by early spaying before the first estrous (Yamazaki et al., 2022).

CMTs range from benign adenomas to highly aggressive carcinomas. For localised lesions, surgical excision with sufficient margins can be curative (Cassali et al., 2020). However, certain aggressive subtypes such as inflammatory mammary carcinomas exhibit extensive local invasion, vascular embolization, and resistance to conventional therapy. A key mechanism underlying metastasis is epithelial-mesenchymal transition (EMT), wherein epithelial cells lose polarity and adhesion and acquire mesenchymal traits. EMT enables tumor invasion, vascular dissemination, and resistance to apoptosis (Priyanka, 2023).

Although chemotherapy and hormonal therapy are integral to current treatment protocols, challenges such as systemic toxicity, chemoresistance, and financial constraints have encouraged the pursuit of phytotherapeutic and herbal approaches as safer, complementary options in veterinary oncology.

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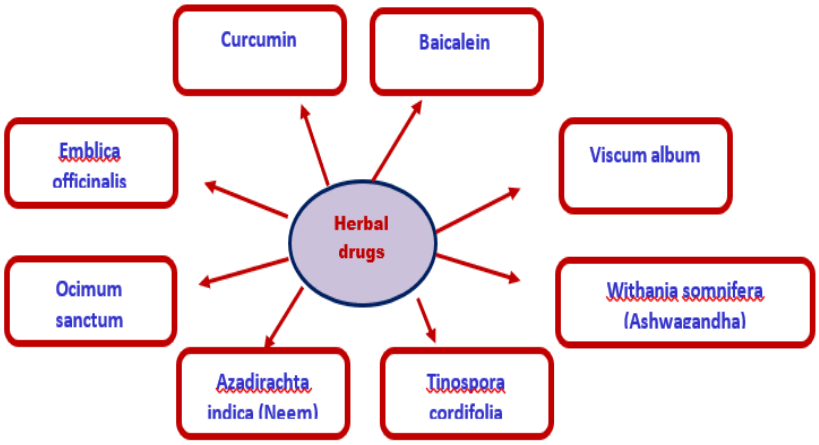
Chemotherapeutic Scenario

Chemotherapy in CMTs is largely empirical, relying on agents like doxorubicin, cyclophosphamide, carboplatin, and 5-fluorouracil (Salas et al., 2019). While these drugs reduce tumor burden, adverse effects such as myelosuppression, hepatotoxicity, and cardiotoxicity restrict their use (Sorenmo et al., 2020). Moreover, expression of P-glycoprotein contributes to multidrug resistance, diminishing effectiveness. Given these challenges, complementary approaches that enhance therapeutic outcomes while minimizing toxicity are gaining importance.

Herbal and Phytotherapeutic Approaches

Numerous preclinical studies have assessed the therapeutic potential of different plant-derived chemicals in canine mammary cancers, showing encouraging effects on tumor development, metastasis, and treatment tolerance (Fig 1). These natural substances are useful supplements or substitutes for traditional treatments since they frequently display multi-targeted modes of action.



Curcumin (Turmeric)

Herbal Approaches to Canine Mammary Tumor Therapy. Curcumin, the major bioactive compound of *Curcuma longa*, exhibits antiproliferative, antioxidant, and pro-apoptotic effects via modulation of NF-κB, p53, and Bcl-2 pathways (Gupta et al., 2012). Curcumin causes caspase-mediated apoptosis and inhibits angiogenesis in canine mammary cancer cell lines. Additionally, research indicates that polyherbal combinations combining rosemary and turmeric increase the production of reactive oxygen species (ROS), block vascular endothelial growth factor, and cause G_2/M cell cycle arrest (Leis Filho et al., 2018).

A study conducted at the College of Veterinary Science, GADVASU, Ludhiana, Punjab, the antineoplastic effects of curcumin and baicalein were reported through their anti-inflammatory and antioxidant mechanisms is a Wister rat mammary tumor model (Priyanka, 2023).

Withania somnifera (Ashwagandha)

Withaferin A, a steroidal lactone from *Withania somnifera*, disrupts cytoskeletal integrity and promotes apoptosis by downregulating vimentin and activating caspase-3 (Widodo et al., 2010). Additionally, it supports tumor regression and strengthens systemic resistance by boosting immunological surveillance through T-cell and macrophage stimulation.

Tinospora cordifolia (Guduchi)

Tinospora cordifolia (giloy) possesses potent antioxidant and immunomodulatory effects. It decreased oxidative stress, systemic inflammation, and neutrophil infiltration in tumor-bearing mice (Garg et al., 2022). In chemotherapy procedures, it is frequently employed as a supportive addition to reduce drug-induced toxicity and boost host immunity.

Azadirachta indica (Neem)

Extracts from *Azadirachta indica* leaves and seeds exert cytotoxic effects by inducing oxidative stress and apoptosis in malignant cells (Agrawal et al., 2020). Neem bioactives modulate angiogenic and inflammatory pathways, making them potential adjuncts in reducing tumor recurrence. However, large-scale veterinary clinical validation is still needed.

ImmuPlus® (Polyherbal Immunostimulant)

Maiti et al. (2009) reported that the administration of ImmuPlus®, a formulation containing *Ocimum sanctum, Emblica officinalis, and Withania somnifera*, resulted in a marked improvement in hematological parameters and attenuation of systemic toxicity induced by doxorubicin during the treatment of canine mammary tumor cases. This reflects the immunomodulatory synergistic effect of the formulation in enhancing host resilience during chemotherapy.

Viscum album (European Mistletoe)

The active constituents of *Viscum album* extract (VAE) are lectins and viscotoxins, which induce apoptosis, stimulate macrophages, and NK cells, and improve the vitality of a patient. In canine oncology, there have been clinical reports of improved recovery and delayed recurrence where these were used in conjunction with surgery or chemotherapy (Schoeffmann et al., 2022).

Enicostema axillare

Ethanolic extracts of Enicostema axillare showed dose-dependent suppression of canine mammary carcinoma cell growth, upregulation of COX-2 and iNOS expression, and elevation of antioxidant enzyme activity (SOD, GPx) at IVRI, Bareilly (IVRI, 2020). These results point to its potential for chemoprevention and oxidative stress regulation.

Clinical and Integrative Insights

Although large-scale randomized veterinary trials remain scarce, small clinical and experimental studies report 30-60% improvement in clinical signs and reduced recurrence when herbal adjuvants are integrated with standard therapy (Maiti et al., 2009). The advantages of herbal drugs in canine mammary tumor management include:

1. Low systemic toxicity compared to synthetic chemotherapeutics.
2. Synergistic action with conventional drugs, enhancing therapeutic efficacy.
3. Antioxidant and anti-inflammatory effects that reduce tumor-associated oxidative damage.
4. Immunomodulatory properties that strengthen host defense mechanisms.
5. Cost-effectiveness and better tolerance, which improve owner compliance in long-term therapy.

CONCLUSION

For the treatment of canine mammary tumors, herbal remedies provide a useful supplemental strategy. Bioactives that work through redox regulation, apoptotic induction, and immunological augmentation include curcumin, neem compounds, etc. When combined with chemotherapy, they can increase the antitumor response, lessen side effects from the medication, and enhance the general health of the patient. Future studies should concentrate on improving bioavailability, standardizing formulations, and conducting controlled clinical trials. Combining evidence-based veterinary oncology with traditional phytomedicine provides a safer and more long-lasting treatment option for dog mammary neoplasia.

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