

Herbal Medicine as a Natural Strategy for Combating Oral Squamous Cell Carcinoma

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Abstract: Oral Squamous Cell Carcinoma (OSCC) remains a major health burden in Karnataka, necessitating innovative, integrative therapeutic strategies. This study employed a multidisciplinary approach combining geospatial mapping, phytochemical screening, and nanotechnology. ArcGIS analysis identified OSCC hotspots across Karnataka, while microbial profiling of saliva samples from patients revealed key pathogenic associations. Ethanolic extracts of *Garcinia gummi-gutta*, *Justicia wynaadensis*, and *Thunbergia fragrans* were prepared and evaluated for antimicrobial, antioxidant, and cytotoxic activities. Among them, *Justicia wynaadensis* extract (JwE) exhibited the highest bioactivity, significantly reducing KB cell viability ($IC_{50} = 86.31 \mu\text{g/mL}$) and inducing apoptosis. High-resolution LC-MS analysis identified bioactive flavonoids and terpenoids as potential anticancer constituents. Using these extracts, TiO_2 nanoparticles (St- TiO_2 NPs) were synthesized and structurally characterized. The nanoparticles demonstrated potent cytotoxic effects against CAL 27 oral cancer cells by inducing reactive oxygen species (ROS) generation, reducing AKT1 expression, and inhibiting cell migration. Anti-angiogenic efficacy was confirmed via the chick chorioallantoic membrane (CAM) assay, and in vivo studies in OSCC-induced hamsters revealed marked tumor regression and histological restoration of buccal tissue. These findings underscore the therapeutic promise of *J. wynaadensis*-derived TiO_2 nanoparticles as a novel, natural, and effective approach for OSCC management, integrating traditional medicine with modern nanomedicine.

Keywords: Oral Squamous Cell Carcinoma (OSCC); St- TiO_2 NPs, *Justicia wynaadensis*; AKT1; Oral Patch

