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PHYTOCHEMICALS FROM AYURVEDIC HERBS: MOLECULAR AND GENETIC BASIS OF ANTICANCER ACTIVITY — MECHANISMS, MOLECULAR TARGETS, AND THERAPEUTIC PERSPECTIVES

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ABSTRACT
Cancer, as a disease, always poses significant global health challenges, prompting the need for effective, less toxic treatments in here. Conventional therapies often face issues such as severe side effects & multi-drug resistance (MDR). Ayurveda, an ancient Indian knowledge-based medicinal system, offers a vast wealth of medicinal herbs with notable pharmacological properties. This review here tends to be examined the anticancer activities of key Ayurvedic phytochemicals-based nature, such as curcumin, withaferin A, nimbolide, berberine, and eugenol. It details their mechanisms in inhibiting cancer, including apoptosis induction, cell cycle arrest, as well as tumor angiogenesis suppression. The review of this paper also mainly discusses the genetic- and epigenetic-based modulation by these compounds and their potential to upgrade the effectiveness of conventional therapies. Additionally, it mainly highlights advances in nanotechnology for better structure and delivery of these phytochemicals, linking traditional medicine with modern cancer care here.

KEYWORDS: Phytochemical activity, anticancer activity, ayurvedic anticancer drugs, action of anticancer activity of ayurvedic drugs.

1. INTRODUCTION

Cancer itself is considered a highly complex genetic based disease marked by the dysregulation of genetic, epigenetic, as well as signaling networks, which leads to unchecked cellular growth & metastasis. Despite constant advances in targeted therapies and immunotherapies, there are traditional treatments like chemotherapy and radiation, where patients suffer from significant side effects & the emergence of chemoresistance (Newman & Cragg, 2020). The need here for a less toxic, pharmacological-based approach has resulted in a focus on natural products, which here have historically contributed to more effective cancer treatments, such as paclitaxel & vincristine (D'Incalci et al., 2005). Ayurveda, a consolidated holistic system of medicine from India, here in this context offers a validated based framework for using botanical formulations to manage chronic diseases based on that, as seen in ancient texts like the Charaka Samhita and Sushruta Samhita in these contexts. Research has always maintained its nature to identify potent phytochemicals from Ayurvedic herbs which to hear that can disrupt oncogenic signaling (Corson & Crews, 2007). Unlike the overly targeted synthetic drugs, Ayurvedic phytochemicals can, in themselves, act as pleiotropic agents, affecting multiple molecular targets to maintain such. This multi-target-based approach is advantageous in oncology, as it addresses the adaptability of tumors in these prospects. This review paper aims here to analyze the anticancer mechanisms of phytochemicals from many of the key Ayurvedic herbs, such as Curcuma longa & Withania somnifera, highlighting more on their genetic & epigenetic targeting and therapeutic potential, thus bridging traditional Ayurvedic practices with modern molecular insights (Amin et al., 2009; Banerjee et al., 2008).

2. Core Ayurvedic Herbs and Key Phytochemicals

The pharmacological efficacy of Ayurvedic botanicals in oncology stems from their complex secondary metabolites—including more on polyphenols, terpenoids, alkaloids, & flavonoids—which here in interact powerfully with biological macromolecular structures. The key nature of phytochemicals derived from highly regarded Ayurvedic herbs includes:

- **Curcumin (*Curcuma longa*):** This golden-yellow-based polyphenol is a foundational based aspects on anti-inflammatory agent & arguably the most extensively studied phytochemical here in cancer research (Aggarwal et al., 2003). By inhibiting more of the major inflammatory transcription-based factors (NF-κB, STAT3, and AP-1), curcumin-based nature effectively neutralizes the chronic and strong inflammation that fuels the tumour microenvironment (Gupta et al., 2012).
- **Withaferin A (*Withania somnifera*):** A structurally related complex steroidal lactone, Withaferin A acts here as a remarkably potent based nature, multi-targeted antineoplastic based nature agent (Singh et al., 2014). It covalently tied to binds to cellular proteins like vimentin & Hsp90, triggering the proteasomal degradation of

oncogenic proteins as well as disrupting the cytoskeletal architecture necessary for malignant metastasis in nature (Vanden Berghe et al., 2012).

- **Nimbolide (*Azadirachta indica*):** Derived here from Neem, this tetranortriterpenoid-based compound demonstrates exceptional anti-proliferative and apoptosis-inducing activity across various cancers based on such aspects (Hao et al., 2014). It modulates the PI3K/Akt & ERK pathways and aggressively downregulates transcription factor-based constants involved in the epithelial-mesenchymal transition (EMT) to halt metastasis-based spread (Elumalai et al., 2012).
- **Berberine (*Tinospora cordifolia*):** This quinoline alkaloid induces stricter cell cycle arrest & apoptosis. By modulating the AMPK energy-sensing enzyme and suppressing cyclin D1 expression, berberine effectively starves cancer cells of the energetic pathways mostly required for rapid division (Lee et al., 2010).

Eugenol and Ursolic Acid (*Ocimum sanctum*): Found here in Holy Basil, these compounds offer robust radioprotective, chemo-preventive, as well as direct tumor-suppressive benefits. They created here most function by mitigating severe natured most intracellular oxidative stress, preventing with delivered early-stage DNA damage, & inducing more lethal apoptotic pathways here specifically in malignant cells (Jantan et al., 2015).

3. Molecular Mechanisms of Anticancer Activity

Ayurvedic phytochemicals here exert more anticancer with detail effects by directly targeting critical nature of biochemical checkpoints of cellular survival, proliferation, angiogenesis, as well as metastasis.

3.1 Induction of Apoptosis (Programmed Cell Death)

These compounds hereby forcefully reactivate more dormant apoptotic signalling via intrinsic & extrinsic pathways. Curcumin here initiates the intrinsic pathway by upregulating pro-apoptotic protein-based structures (Bax, Bak, Puma) as well as severely downregulating anti-apoptotic survival proteins (Bcl-2, Bcl-xL, Survivin) (Teiten et al., 2010). This shift compromises the mitochondrial membrane potential, releasing more cytochrome c & triggering the lethal caspase-9 cascade (Pan et al., 2008). Withaferin A induces more caspase-dependent apoptosis by maintaining the reactive oxygen species (ROS)- based nature that irreversibly damages mitochondrial membranes here (Hahm et al., 2011). Extrinsically, nimbolide sensitizes cells to TRAIL-mediated apoptosis by upregulating death receptors (DR4/DR5) and hereby completely suppressing the anti-apoptotic shield c-FLIP (Hao et al., 2014).

3.2 Cell Cycle Arrest

Phytochemicals here halt unchecked mostly tumor growth by most strictly modulating the cell cycle machinery in this perspective. Curcumin actively here induces G2/M phase arrest by downregulating with cyclin-B1 and cdc2 kinase here while upregulating tumor-suppressive inhibitors p21 & p27 (Aggarwal et al., 2003). Berberine here forces a rigid G1-phase arrest by activating here in the AMPK signaling cascade here to suppress cyclin D1 & CDK4 (Lee et al., 2010). These nature of the blockades grant cells with time for DNA repair or force irreparably by damaged cells into more apoptosis.

3.3 Inhibition of Angiogenesis

Curcumin curtails tumor angiogenesis by directly inhibiting HIF-1α transcriptional activity, to maintain it completely preventing the secretion of VEGF and bFGF (Gupta et al., 2012). Similarly, Withaferin A blocks endothelial cell proliferation & tube formation by directly targeting VEGFR2 & crippling its downstream intracellular signalling cascade-based structure (Vanden Berghe et al., 2012).

3.4 Suppression of Metastasis and EMT

These nature of compounds prevent systemic always to carry with spread by vigorously suppressing the Epithelial-Mesenchymal Transition (EMT). Nimbolide here represses master EMT transcription factors (Twist, Snail, Slug), restoring more of the protective E-cadherin while suppressing more mesenchymal markers like N-cadherin & vimentin (Elumalai et al., 2012). Furthermore, here are more on nature phytochemicals prevent based nature physical tumor invasion by inhibiting here in the secretion of extracellular matrix-degrading enzymes, mostly on thr notably MMP-2 and MMP-9 (Kunnumakkara et al., 2008).

4. Genetic and Epigenetic Targets

Beyond here more natured basedtransient cytoplasmic interactions, Ayurvedic phytochemicals orchestrate profound genomic as well as epigenomic alterations, actively reversing the most aberrant transcriptomic landscapes characteristic of malignant cells.

4.1 Modulation of Oncogenes and Tumor Suppressors

The p53-based tumor suppressor is a critical pharmacological target here. Curcumin, a chemically based, stabilizes wild-type p53 & enhances more of its baseline transcriptional activity by inhibiting its primary negative regulator, MDM2 (Pan et al., 2008). In aggressive cancers with most mutant p53, Withaferin A induces the physical depletion of the mutant protein via autophagic as well as proteasomal degradation (Singh et al., 2014). Additionally, these phytochemicals actively, in this nature downregulate prominent oncogenes, including here with c-Myc, Her2/neu, & mutated Ras, depriving tumors of fundamental survival signals for these purposes.

4.2 Epigenetic Modifications

Curcumin always acts as a potent nature here with epigenetic modulator and DNA methyltransferase (DNMT) inhibitor. By strongly suppressing DNMT activity, curcumin reverses the silencing caused by promoter hypermethylation of vital genes like RASSF1A and Nrf2 (Reuter et al., 2011). Furthermore, curcumin functions as a natural inhibitor of histone deacetylases (HDACs). This promotes here particularly an open chromatin-based architecture, facilitating the essential nature of transcription of suppressed tumor suppressor genes (Reuter et al.,

2011).

4.3 MicroRNA (miRNA) Regulation

Phytochemicals here are considered to more powerfully reprogram the cellular miRNA milieu. Curcumin severely downregulates miR-21, a well-characterized oncomiR promoting metastasis & chemoresistance, while simultaneously here on upregulating protective, tumor-suppressive miRNAs such as more with miR-15a, miR-16, miR-22, and the let-7 family (Sarkar et al., 2009).

Table 1: Key Ayurvedic Phytochemicals, their Botanical Sources, and Primary Molecular Targets in Cancer

Phytochemical	Botanical Source (Ayurvedic Herb)	Primary Molecular Targets / Pathways	Demonstrated Efficacy (Cancer Types)
Curcumin	Curcuma longa (Turmeric)	NF-κB, STAT3, AP-1, VEGF, p53, DNMT, HDAC, miR-21	Breast, Colon, Prostate, Pancreatic, Lung, Ovarian
Withaferin A	Withania somnifera (Ashwagandha)	Vimentin, Hsp90, Caspase-3/9, NF-κB, mutant p53	Breast, Ovarian, Prostate, Glioblastoma, Melanoma
Nimbolide	Azadirachta indica (Neem)	PI3K/Akt, ERK, Twist, Snail, MMP-2/9, DR4/5	Colon, Prostate, Breast, Hepatocellular, Cervical
Berberine	Tinospora cordifolia (Guduchi)	AMPK, Cyclin D1, CDK4, mTOR, Bcl-2	Lung, Gastric, Melanoma, Leukemia, Osteosarcoma
Eugenol / Ursolic Acid	Ocimum sanctum (Tulsi)	ROS generation, COX-2, p21 upregulation, Nrf2	Skin, Gastric, Breast, Cervical, Oral Squamous

Table 2: Genetic and Epigenetic Alterations Modulated by Ayurvedic Phytochemicals

Target Category	Specific Gene / Element	Modulating Phytochemical	Outcome of Modulation
Tumor Suppressors	p53, p21, p27	Curcumin, Ursolic Acid, Berberine	Stabilization and potent transcriptional activation; robust cell cycle arrest at G2/M or G1.
Oncogenes	c-Myc, Her2/neu, mutant p53	Withaferin A, Nimbolide	Severe downregulation and rapid proteasomal degradation; total loss of oncogenic signaling cascades.
Epigenetic (Methylation)	DNMT1, DNMT3a/b	Curcumin, Eugenol	Inhibition of DNA methylation enzymes; complete re-expression of previously silenced tumor suppressor genes.
microRNAs (miRNAs)	miR-21 (down), let-7 (up)	Curcumin, Berberine, Nimbolide	Suppression of highly destructive oncomiRs and vital restoration of complex tumor-suppressive miRNA networks.

5. Synergistic Effects, Bioavailability, and Therapeutic Perspectives

Translating here with most Ayurvedic phytochemicals into these in mainstream clinical oncology requires addressing with their synergistic integration with standard based treatments & overcoming pharmacokinetic limitations.

5.1 Synergism and Overcoming Chemoresistance

These compounds serve solely as potent chemosensitizers against multidrug resistance (MDR) driven by efflux pumps like P-gp & survival pathways like NF-κB. Curcumin-based compounds effectively downregulate P-gp & inhibits chemotherapy-induced NF-κB hyperactivation in this nature. When co-administered with standard chemotherapeutics, curcumin lowers the cellular apoptosis threshold, allowing for significant dose here more of the reductions of toxic synthetic drugs while actively enhancing overall tumor burden reduction (Kunnumakkara et al., 2008). Similarly, Withaferin A exhibits profound synergism, mainly with paclitaxel, in aggressive lung & extremely natured herewith resistant ovarian cancer models, effectively obliterating cellular resistance-based mechanisms in these models (Youns et al., 2010).

5.2 Bioavailability and Advanced Nano-formulations

Despite the immense nature of in vitro efficacy, the most prospects for broad nature in here clinical utility of curcumin and withaferin A are mainly historically limited by poor aqueous solubility, rapid systemic clearance, and low targeted cellular uptake (Anand et al., 2008). To more of a circumvent these massive pharmacokinetic barriers, here advanced nanotechnology—including herein biocompatible liposomes and solid lipid nanoparticles—is revolutionizing more with their clinical administration (Mandal et al., 2020). Liposomal formulations based on nature vastly enhance biological half-life and tissue penetration, while active targeting mechanisms ensure all these potent phytochemicals are delivered directly into the tumor core, effectively eliminating off-target systemic exposure.

6. Clinical Translation and Future Directions

The current nature of preclinical & clinical data here strongly supports the integration of Ayurvedic phytochemicals into modern medicine, yet here the rigorous human trials remain crucial in this nature. Ongoing phase I & II trials are assessing specialized curcumin-based formulations for their own safety & efficacy in treating premalignant lesions as well as enhancing chemotherapy in aggressive cancers in this nature (Frenkel et al., 2006). Preliminary based nature here to seen through results indicate that these compounds are well-tolerated, with minimal adverse effects. Future oncological research will benefit from overly uses of advanced systems biology, computational drug discovery, & AI, allowing for more precise mapping of Ayurvedic extracts' interactions in this scenario. Personalized oncology approaches, such as ex vivo tumor organoids, will further validate the effectiveness of Ayurvedic compounds against here on individual tumors, bridging more ancient, nature-based practices with modern precision medicine.

7. CONCLUSION

The exploration-based nature of the bioactive phytochemical structures from Ayurvedic herbs represents a lot of transformative avenues here in oncological research. Compounds such as curcumin & withaferin A are recognized more or less as potent pharmacological agents rather than merely alternative remedies; they more effectively target the structured molecular mechanisms of cancer by inducing apoptosis, blocking mutated cell cycles, inhibiting metastasis, and reversing genetic abnormalities. The integrative nature of traditional Ayurvedic knowledge with modern nanotechnology and genomic science suggests significant clinical potential herein.

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