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Anticancer and Cytotoxic Natural Compounds from Central Asian Medicinal Plants: A Narrative Review

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ABSTRACT: Plant-derived natural products continue to supply a substantial proportion of clinically used and investigational anticancer agents, yet the medicinal flora of Central Asia, and Uzbekistan in particular, remains comparatively underexplored as a source of such compounds relative to its exceptional botanical diversity. This review synthesises evidence on cytotoxic and antitumour secondary metabolites characterised from Central Asian plant genera, drawing on both classical phytochemical work carried out largely by regional research groups and more recent, internationally published studies. We discuss flavonoids from Scutellaria immaculata and S. ramosissima, phytoecdysteroids isolated from several Silene species with demonstrated in vitro antitumour and antioxidant activity, sesquiterpene coumarins from Ferula species with documented cytokine-modulating and cytotoxic effects, essential-oil constituents from aromatic Tajik plants active against HeLa, Caco-2 and MCF-7 cancer cell lines, and anticancer polysaccharides and proteins isolated from medicinal macrofungi native to the region's forest ecosystems. Across these taxa, the dominant chemical classes with documented cytotoxic activity include flavonoids, phytoecdysteroids, sesquiterpene coumarins and fungal polysaccharide-protein complexes, several of which additionally display antioxidant or immunomodulatory properties that may act synergistically with direct cytotoxicity. We conclude that Central Asian flora and associated macrofungi constitute a genuine, still substantially underexploited source of candidate anticancer natural products, but that the evidence base remains almost entirely preclinical, in vitro and mechanistically incomplete, and that structure-activity elucidation, in vivo efficacy testing and eventual clinical evaluation represent the principal directions required to translate this regional phytochemical heritage into oncological application.

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1. INTRODUCTION

Natural products and their structural derivatives account for a substantial share of anticancer agents currently in clinical use or under active investigation, reflecting the chemical diversity that plant secondary metabolism has generated over evolutionary timescales in response to herbivory, pathogen pressure and environmental stress [1]. Central Asia, encompassing Uzbekistan, Kazakhstan, Kyrgyzstan, Tajikistan and Turkmenistan, has been repeatedly described in the recent literature as one of the least ethnopharmacologically documented regions globally relative to the size and endemism of its flora, despite a long, continuous tradition of medicinal plant use extending back along Silk Road trade routes [2]. Within this broader gap, systematic characterisation of anticancer and cytotoxic natural products from Central Asian plant material has historically depended heavily on the work of a small number of regional phytochemistry groups, whose findings, published mainly in specialist natural-product journals, have not always been widely integrated into the international oncology-focused natural-products literature.

A substantial body of foundational phytochemical work on Uzbek flora, carried out over more than two decades by research groups centred on institutions in Tashkent, has characterised flavonoids, phytoecdysteroids and terpenoids from numerous native genera, several of which possess documented in vitro cytotoxic or antitumour activity [3]. This review synthesises this regional evidence base together with more recent studies published internationally, with the aim of providing an integrated account of which Central Asian plant taxa and compound classes currently possess the strongest documented anticancer or cytotoxic evidence, and of identifying priority directions for further mechanistic and translational investigation.

2. METHODS

This narrative review draws on peer-reviewed phytochemical and pharmacological studies reporting cytotoxic, antitumour or anticancer activity of plant and fungal material native to or traditionally used in Central Asia, identified through searches of PubMed, Scopus and Google Scholar using combinations of the terms "Central Asia", "Uzbekistan", "Tajikistan", "cytotoxic", "anticancer", "antitumour", together with genus-specific search terms for the taxa discussed below. Given the substantial body of regional phytochemical literature published in specialist natural-product-chemistry journals, studies reporting primary in vitro cytotoxicity data (typically cancer cell-line viability assays with reported IC50 values) were prioritised over purely descriptive ethnobotanical sources.

3. CYTOTOXIC COMPOUND CLASSES FROM CENTRAL ASIAN FLORA

3.1 Flavonoids from Scutellaria Species

Several Scutellaria (Lamiaceae) species native to Central Asia, including S. immaculata and S. ramosissima, have been characterised as sources of flavonoids such as scutellarin, chrysin, apigenin and related apigenin derivatives, compounds that have been evaluated for a range of biological activities including cytotoxic effects against cancer cell lines [4]. A dedicated 2014 study documented both the ethnobotanical use and the cytotoxic activity of a broader set of native Lamiaceae species from Uzbekistan, providing one of the more systematic regional evaluations linking traditional use to laboratory-confirmed antiproliferative activity within this plant family [5]. Related work on Scutellaria species from neighbouring regions has separately demonstrated pro-apoptotic effects of Scutellaria root extracts against multiple cancer cell lines, a pattern broadly consistent with the wider literature on Scutellaria-derived flavonoids as cytotoxic agents [6].

3.2 Phytoecdysteroids from Silene Species

Phytoecdysteroids, polyhydroxylated steroidal compounds structurally related to insect moulting hormones, have been extensively characterised from several Silene (Caryophyllaceae) species collected in Uzbekistan, including S. viridiflora and S. guntensis, by a research group that has published a sustained series of studies on this genus over more than a decade [7]. Ecdysteroid-containing extracts of S. viridiflora have demonstrated antitumour activity in addition to their better-known adaptogenic and actoprotective properties, while phytoecdysteroids isolated from S. guntensis have shown measurable in vitro cytotoxic activity alongside antioxidant effects, with the saponin fraction of these extracts specifically implicated as a likely contributor to the observed cytotoxicity [8]. Related ecdysteroid-bearing species, including the Uzbek endemic Ajuga turkestanica, from which the ecdysteroid turkesterone was first isolated, have similarly demonstrated weak but measurable radical-scavenging activity that may complement direct cytotoxic mechanisms in a broader antitumour context [9].

3.3 Sesquiterpene Coumarins from Ferula Species

The genus Ferula, well represented across Central Asia and discussed in detail in our companion ethnopharmacological review of the region's flora, is characterised chemically by oleo-gum-resins rich in sesquiterpene coumarins, several of which possess documented cytotoxic and antiviral activity. Coumarins and a bicoumarin isolated specifically from Ferula sumbul were shown, in early but frequently cited work, to possess anti-HIV activity together with the ability to inhibit cytokine release, indicating that this compound class exerts biological effects extending beyond direct cytotoxicity toward broader immunomodulatory and antiviral mechanisms relevant to cancer-associated inflammation [10]. More recent phytochemical work on Ferula-derived sesquiterpene coumarins, discussed in greater detail elsewhere, has demonstrated potent cytotoxicity of specific isolated compounds such as gummosin against colorectal carcinoma cell lines in vitro [11], reinforcing sesquiterpene coumarins as a chemical class of sustained anticancer interest within this genus.

3.4 Essential-Oil Constituents from Aromatic Central Asian Plants

Essential oils from aromatic plants traditionally used across the wider Central Asian region, including Tajikistan, have been characterised for cytotoxic activity against established human cancer cell lines. The essential oil of Girardinia fragrantissima, a plant distributed across Afghanistan, Kyrgyzstan, Uzbekistan and Tajikistan and traditionally used as a culinary spice, demonstrated cytotoxicity against HeLa, Caco-2 and MCF-7 cancer cell lines, with the lowest half-maximal inhibitory concentration observed against MCF-7 cells, an effect attributed principally to its long-chain aliphatic aldehyde constituents [12]. The same regional phytochemical survey documented cytotoxic activity of germacrene D against PC-3 prostate cancer cells and of caryophyllene oxide against MCF-7, PC-3 and Hep-G2 cell lines, while noting that the related compound β-caryophyllene, though not independently strongly cytotoxic, has been reported to potentiate the anticancer activity of other co-administered compounds [12].

3.5 Anticancer Compounds from Medicinal Macrofungi

Beyond vascular plants, medicinal macrofungi documented in Uzbekistan's forest ecosystems represent a further source of characterised anticancer natural products. A systematic field survey of medicinal macrofungi in Uzbekistan catalogued several species with documented anticancer properties in the broader mycological literature, including Lentinus tigrinus, from which a soluble protein fraction has demonstrated antiproliferative and cytotoxic activity against PC-3 prostate cancer cells, and separately, extracts with cytotoxic activity against MCF-7 breast cancer cells while posing comparatively little risk to humans when consumed in typical dietary amounts [13]. The same survey identified additional species, including Inonotus hispidus, whose bioactive constituents hispolon and hispidin have been associated with antitumour, antiproliferative and cytotoxic effects alongside immunomodulatory and natural-killer-T-cell-stimulating activity, illustrating that anticancer potential within this fungal group is frequently accompanied by, and may mechanistically interact with, immune-modulating properties [13].

4. CROSS-CUTTING MECHANISTIC THEMES

Across the plant and fungal taxa reviewed, several recurring patterns emerge. Flavonoid- and phytoecdysteroid-rich taxa, exemplified by Scutellaria and Silene species respectively, frequently combine measurable cytotoxic activity with antioxidant and, in some cases, immunomodulatory or adaptogenic properties, suggesting that their anticancer potential may operate through multiple, partially overlapping mechanisms rather than a single well-defined molecular target [7,8]. Sesquiterpene coumarins from Ferula similarly combine direct cytotoxicity against specific cancer cell lines with documented antiviral and cytokine-modulating effects, a combination of properties of particular relevance given the increasingly recognised role of chronic inflammation in tumour promotion [10,11]. Medicinal macrofungi appear to contribute a mechanistically distinct set of anticancer constituents, principally polysaccharides and bioactive proteins, that act at least partly through immunomodulation and natural-killer-cell activation rather than through direct cytotoxic mechanisms alone [13].

5. CHALLENGES AND FUTURE DIRECTIONS

Several limitations constrain the translational potential of the evidence reviewed here. Most reported cytotoxicity data derive from crude extracts or partially purified fractions tested against a limited panel of established cancer cell lines, most commonly MCF-7, HeLa and PC-3, without consistent comparison against non-malignant control cell lines, which limits confident interpretation of selectivity between cytotoxicity toward malignant versus healthy tissue [12,13]. Standardised potency thresholds exist in the broader natural-products literature, with crude extracts generally considered promising anticancer

candidates at half-maximal inhibitory concentrations below approximately twenty to thirty micrograms per millilitre, yet these thresholds are inconsistently applied and reported across the regional Central Asian literature reviewed here, complicating direct comparison between studies [14]. Furthermore, essentially none of the compounds discussed in this review have progressed beyond in vitro cell-line testing toward in vivo efficacy studies or any form of clinical evaluation, and detailed structure-activity relationship studies capable of guiding rational chemical optimisation remain scarce for most of the specific compounds identified from Central Asian sources specifically. Addressing these gaps through standardised, comparative in vitro screening panels, mechanistic studies clarifying molecular targets, and eventual in vivo validation represents the clearest path toward translating this substantial but fragmented regional phytochemical evidence base into genuine oncological application.

6. CONCLUSION

Central Asian medicinal flora and associated macrofungi have yielded a phytochemically diverse set of compounds with documented in vitro cytotoxic or antitumour activity, spanning flavonoids from Scutellaria, phytoecdysteroids from Silene and related genera, sesquiterpene coumarins from Ferula, essential-oil constituents from aromatic Tajik plants, and polysaccharide-protein complexes from medicinal macrofungi. This evidence base, built substantially on sustained regional phytochemical research over the past two decades, remains almost entirely preclinical and mechanistically incomplete relative to the scale of the region's underlying botanical diversity. Realising the anticancer potential of this natural resource will require expanded international collaboration, standardised cytotoxicity screening methodology, and a sustained research trajectory extending from compound isolation toward mechanistic, in vivo and ultimately clinical evaluation.

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