Title: Repurposing 3-Acetyl-11-Keto-β-Boswellic Acid for Chemotherapy-Related Cognitive Impairment: A Dual-Action Neuroprotective and Anticancer Strategy

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Dear Editor

Chemotherapy-related cognitive impairment (CRCI), commonly referred to as *chemobrain*, is among the most prevalent and disabling long-term toxicities of systemic chemotherapy, substantially impairing quality of life and functional independence in cancer survivors. Despite increasing recognition of its clinical significance, no pharmacological intervention has yet been approved for its prevention or treatment. Contemporary evidence indicates that CRCI results from the convergence of neuroinflammation, oxidative stress, mitochondrial dysfunction, impaired neurogenesis, synaptic dysfunction, and neuronal apoptosis, highlighting the need for therapeutic approaches capable of modulating multiple interconnected pathogenic pathways rather than a single molecular target [1-4]. Nevertheless, the major challenge in developing neuroprotective strategies for oncology extends beyond the complexity of CRCI itself. A persistent concern is that protecting normal neural tissue may inadvertently reduce the cytotoxic efficacy of chemotherapy. Therefore, an ideal supportive therapy should preserve cognitive function while remaining fully compatible with—and preferably enhancing—the antitumor activity of anticancer treatment [1-4].

Within this framework, 3-acetyl-11-keto-β-boswellic acid (AKBA), the principal bioactive pentacyclic triterpenoid of *Boswellia serrata*, deserves consideration as a promising drug-repurposing candidate. Although AKBA has not yet been investigated in dedicated CRCI models, accumulating evidence from experimental models of neuroinflammation and neurodegenerative disorders demonstrates that it suppresses neuroinflammation and oxidative stress, preserves mitochondrial integrity, activates endogenous antioxidant defenses, attenuates neuronal apoptosis, and improves cognitive performance through modulation of pathways that substantially overlap with the biological mechanisms implicated in CRCI [5-8]. These findings provide a compelling biological rationale for evaluating AKBA in chemotherapy-induced cognitive dysfunction rather than constituting direct evidence of efficacy.

Equally important, AKBA possesses intrinsic anticancer properties that distinguish it from most candidate neuroprotective agents. Experimental studies have demonstrated that AKBA suppresses tumor cell proliferation, induces apoptosis, inhibits invasion and metastatic signaling, overcomes therapeutic resistance, and enhances the efficacy of conventional anticancer therapies through modulation of multiple oncogenic pathways, including NF-κB, PI3K/Akt, Notch, and other survival signaling cascades [9-12]. This dual pharmacological profile raises the possibility that neuroprotection and preservation of antitumor efficacy need not represent competing therapeutic goals. Instead, AKBA may exemplify a new class of adjunctive supportive agents capable of simultaneously mitigating treatment-related neurotoxicity while complementing cancer therapy.

Although this hypothesis requires experimental validation, the convergence of mechanistic evidence from neuroscience and oncology provides a strong rationale for translational investigation. Future studies should evaluate AKBA in clinically relevant tumor-bearing models of CRCI using both cognitive and oncological endpoints to determine whether neuroprotection can be achieved without compromising—and potentially improving—the efficacy of chemotherapy.

Confirmation of this concept would not only support repurposing AKBA for CRCI but also establish a broader paradigm for developing supportive cancer therapies that protect normal tissues while reinforcing anticancer responses.

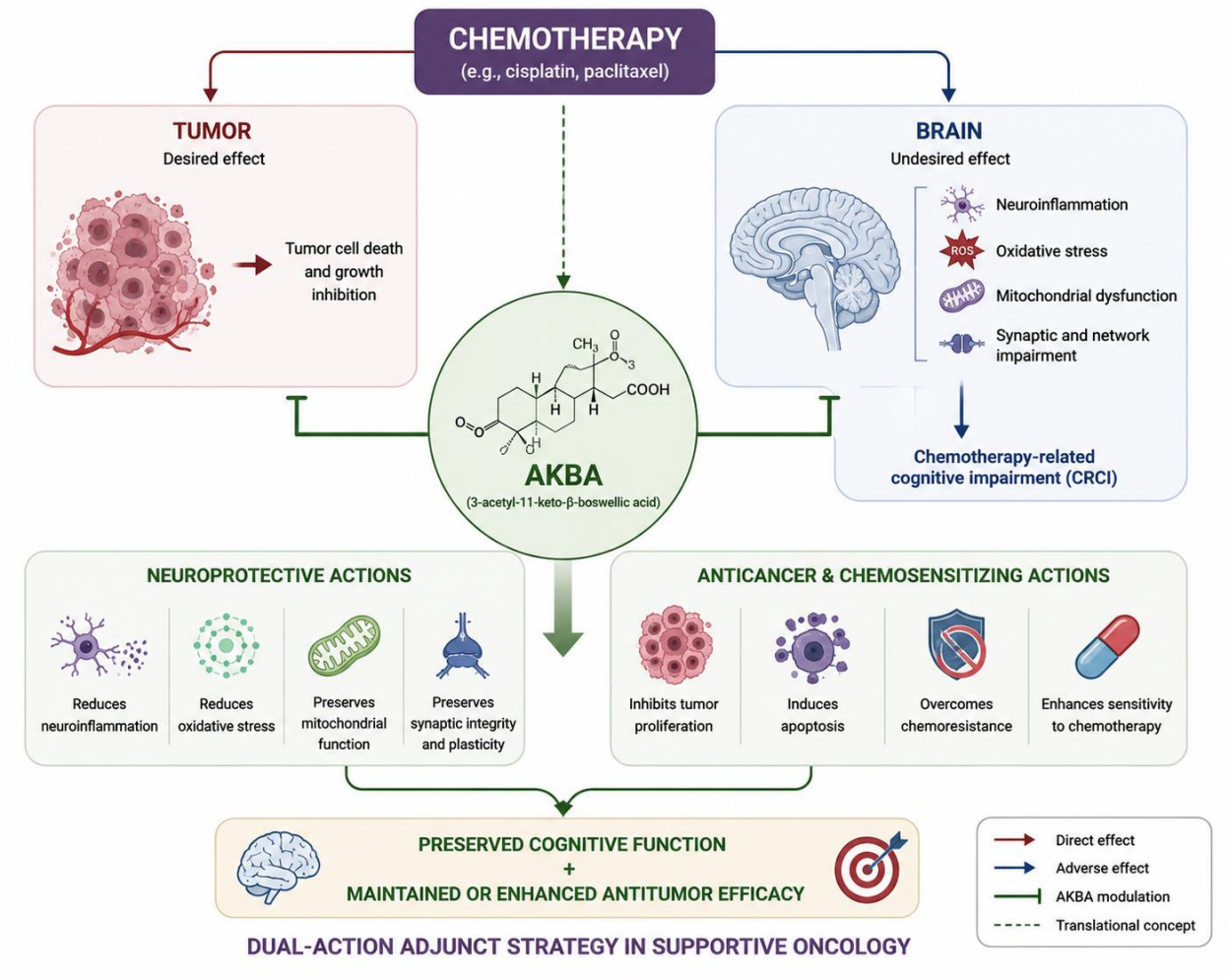

Figure 1. Conceptual framework illustrating the proposed dual-action role of AKBA in chemotherapy-related cognitive impairment. Chemotherapy exerts antitumor effects but also induces multiple mechanisms implicated in CRCI, including neuroinflammation, oxidative stress, and mitochondrial dysfunction. AKBA is hypothesized to simultaneously attenuate these neurotoxic processes while maintaining or enhancing the anticancer efficacy of chemotherapy through its intrinsic antitumor and chemo-sensitizing activities. This dual pharmacological profile forms the central hypothesis of the present commentary.

Author Contributions

Conceptualization, Data curation, Investigation, Supervision, Writing—original draft, Writing—review & editing: Zahra Nazari Taloki.

Conflicts of Interest

The author has no potential conflicts of interest to disclose.

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