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# New Insights into Secondary Metabolite Potential in *Hypericum Perforatum*, UPLC-ESI-MS/MS to Novel Phytochemical Discovery with Bioactivity Assessment

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Different anatomical components of *Hypericum perforatum* (*H. perforatum*) have been utilized by humans for generations as a natural remedy with pharmacological attributes. This work aimed to investigate the secondary metabolite potential of *H. perforatum* from algeria using LC-ESI-MS/MS to determine its phytochemical profile. LC-ESI-MS/MS analysis revealed 22 components, with isoquercitrin being the most abundant bioactive compound at a concentration of 4162 µg/g. The total phenolic and flavonoid contents were also quantified, with TPC equal 171.54 ± 0.79 mg GAE/g and TFC equal 144.26 ± 14.3 mg QE/g. The antioxidant capacity of the extract was evaluated using in vitro assays, showing strong activity with an ABTS $IC_{50}$ of 0.173 mg/mL. The antiproliferative potential of the methanolic extract was assessed by the MTT assay on CAPAN-1, DLD-1, and the healthy L929 cell line. The extract exhibited significant antiproliferative effects on CAPAN-1 and DLD-1 cells, with $IC_{50}$ values of 0.807 ± 0.06 mg/mL and 0.953 ± 0.03 mg/mL, respectively, whereas no cytotoxicity was observed on L929 cells. Furthermore, SwissADME was used to evaluate the pharmacokinetics and drug-likeness of the main compounds. These findings enhance the understanding of *H. perforatum* and may support its prospective applications in pharmaceutical and cosmetic industries.

## 1. Introduction

According to a literature review, *Hypericum* is a notable genus within the *Hypericaceae* family, consisting of over 500 species[1] categorized into 36 sections (Robson, 2006).[2] *Hypericum perforatum* (*H. perforatum*), or St. John's wort, has been utilized in both traditional and contemporary medicine as a treatment for hemorrhoids, diarrhea, and ulcers,[3,4] in addition to addressing bruises, burns, swellings, eczema, and psychological disorders including anxiety, neuralgia, and mild to moderate depression.[5] It has also been utilized to address fibrositis, sciatica, and menopausal neurosis[6] Moreover, it has been employed to promote vasodilation,[7] and prior studies have established its efficacy in addressing chronic stress, Alzheimer's disease, and Parkinson's disease.[8,9] The red pigments of *H. perforatum*, hypericin and pseudohypericin, have been documented to possess various bioactivities, including antidepressant, antioxidant, anti-inflammatory, antiviral, antimicrobial, cytotoxic, wound-healing, analgesic, hepatoprotective, and antibacterial effects,[10,11] alongside tyrosinase and cholinesterase inhibitory activities[12,13] and antiretroviral and anticancer properties.[14–17]

Currently, the investigation of antioxidant capacities has become an important topic as the adopted lifestyles are favored to lead to improved health conditions. Consequently, the attention toward botanical products as a source of natural antioxidants has increased. According to some studies, natural antioxidants, including phenolic phytochemicals, might be promising agents for cancer chemoprevention and cancer treatment.[18] The antitumor activity of *H. perforatum* has been investigated mainly with photodynamic therapy.[19,20] A more recent study also reported the discovery of two new compounds in *H. perforatum*, 2,6,9-trimethyl-8-decene-3,5-dione and 3,7,10-trimethyl-9-undecane-4,6-dione.[21] However, the amount of different bioactive compounds in *H. perforatum* may vary

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