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Khaya grandifoliola C.DC: A potential source of active ingredients with pharmacological activities

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Statement of the Problem: *Khaya grandifoliola* (Meliaceae) is used in Cameroonian traditional medicine for the treatment of jaundice and others liver related diseases. Scientific reports supporting its use in folk medicine have been documented through laboratory experiments using extract and compounds from stem bark of the plant. Antiviral, hepatoprotective and anti-inflammatory activities as well as the related molecular mechanisms were investigated.

Methodology: Dried bark powder was extracted in methylene chloride/methanol (v/v) system and separated by flash chromatography. The hepatoprotective activity of the fractions obtained was tested by assessing their effect against H₂O₂, cisplatin and acetaminophen (APAP)-induced hepatotoxicity in HC-04 and L-02 cells line. The antiviral (hepatitis C virus) activity was assessed by measuring infection and replication rates in Huh-7 cells using subgenomic replicon, HCV-pseudotyped and HCVcc particles. The anti-inflammatory activity was evaluated against lipopolysaccharide (LPS)-induced inflammation in raw 264.7 macrophages model. Cell viability was assessed by MTT assay and the chemical composition of the most active fraction was analyzed by GC-MS, HPLC and NMR.

Findings: Five fractions of different polarities were obtained. One (KgF25), showed the strongest hepatoprotective, antiviral and anti-inflammatory activities at non-toxic concentration. The hepatoprotective effect of KgF25 was associated to the inhibition of CYP2E1 expression and c-JNK phosphorylation, and the induction of Mkp-1 expression and nuclear translocation of Nrf2. This fraction also inhibited HCV infection by mostly targeting entry and replication step. Its antiviral effect was mediated by the transcriptional up-regulation of hme oxygenase-1 and interferon antiviral response genes. This fraction also showed anti-inflammatory effect through inhibition of nitric oxide production, P38MAP-Kinase and JNK3 enzymes activities and mRNA expression of iNOS and major pro-inflammatory cytokines (TNF- α and IL-1 β). In addition, six compounds exhibited the aforementioned activities were identified from KgF25.

Conclusion & Significance: These findings demonstrate that *K. grandifoliola* is a potential source of active ingredients bearing pharmacological activities.