ABSTRACT

This study employs a reverse pharmacology approach to scientifically validate the cardioprotective and antihypertensive effects of Khamira Gaozaban Sada (KGS), a traditional Unani remedy historically used for 'weak heart,' likely referring to cardiac failure.

The anti-hypertensive activity of KGS and other Unani formulations (KAS, DMM, MSR, HJ) was assessed using the L-NAME-induced hypertensive rat model. While DMM significantly reduced systolic blood pressure (SBP) and plasma nitrite levels, KGS showed increased SBP but significantly altered plasma potassium, adrenaline, and noradrenaline levels, suggesting a central sympathomimetic mechanism. Further evaluation in a Doxorubicin-induced cardiac hypertrophy model revealed that high-dose KGS (2000 mg/kg) ameliorated adverse cardiac parameters, including SBP, QTc, HW/TL ratio, MDA levels, and histopathological changes. Metabolite profiling identified bioactive compounds like Rosmarinic Acid (RA) and Trehalose (TR), with Tiliroside showing strong ACE-binding affinity in docking studies.

KGS also demonstrated significant cardioprotection in Isoproterenol-induced hypertrophy models by improving echocardiographic parameters, reducing oxidative stress, and modulating Ang-II, aldosterone, and intracellular calcium. In vitro studies confirmed protective effects against cytotoxicity and calcium overload in H9C2 cells, with minimal CYP enzyme inhibition, suggesting a low risk of drug interactions. To enhance bioavailability and stability, KGS-loaded chitosan-coated alginate beads were formulated using a Box-Behnken design. Optimized formulations (F13) showed high encapsulation efficiency, pH-sensitive swelling, and sustained release of RA and TR. Structural and thermal analyses (FTIR, TGA, SEM) confirmed successful encapsulation and bead integrity.

In conclusion, the findings validate KGS as a cost-effective cardioprotective agent, confirming its traditional use and supporting its integration into modern therapies and targeted drug delivery systems.

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