基于网络药理学和分子对接研究大黄治疗膝关节炎的分子机制

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摘 要：目的 利用网络药理学和分子对接研究大黄治疗膝关节炎的分子机制。**方法** 通过 TCMSP、PubChem、Swiss 数据库收集到大黄的活性成分和潜在作用靶点。利用 GeneCards、OMIM、DisGeNET 数据库检索得到膝关节炎的相关靶点。利用 Venny 2.1 绘制韦恩图，得到大黄治疗膝关节炎的交集靶点。基于 STRING 数据库，运用 Cytoscape 3.10 软件制作“药物－活性成分－潜在靶点－疾病”网络图，用拓扑分析筛选出核心靶点。利用 DAVID 数据库进行基因本体（GO）富集分析和京都基因与基因组百科全书（KEGG）通路富集分析，并通过 Discovery Studio 软件进行分子对接。**结果** 共筛选出 16 个大黄活性成分，包括大黄素、β-谷甾醇、大黄酸、大黄素甲醚等，筛选出蛋白激酶 B1（Akt1）、基质金属蛋白酶 9（MMP9）、表皮生长因子受体（EGFR）、原癌基因酪氨酸蛋白激酶（SRC）、胱天蛋白酶 3（CASP3）等核心靶点。大黄治疗膝关节炎的信号通路主要富集于癌症中的蛋白多糖通路、癌症通路、内分泌抵抗通路、前列腺癌通路、表皮生长因子受体信号通路、焦点黏附通路、人类巨细胞感染通路等。分子对接显示核心成分大黄素、β-谷甾醇、大黄酸、大黄素甲醚等与核心靶点 Akt1、MMP9、EGFR、SRC、CASP3 等对接程度良好。**结论** 大黄中大黄素、大黄酸等有效成分可能通过作用于 Akt1、MMP9、EGFR 等靶点调节多条信号通路，达到治疗膝关节骨性关节炎的作用。

关键词：大黄；膝关节炎；网络药理学；分子对接；大黄素；β-谷甾醇；大黄酸
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Molecular mechanism of *Rhei Radix* et *Rhizoma* in treatment of knee osteoarthritis based on network pharmacology and molecular docking

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Abstract: Objective To study the molecular mechanism of *Rhei Radix* et *Rhizoma* in treatment of knee osteoarthritis. **Methods** The active ingredients and potential targets of *Rhei Radix* et *Rhizoma* were collected through TCMSP, PubChem, and Swiss databases. GeneCards, OMIM, and DisGeNET databases were used to search the related targets of knee arthritis. The intersection target of *Rhei Radix* et *Rhizoma* in treatment of knee arthritis was obtained by using Venny 2.1 to draw Venn diagram. Based on STRING database, the network diagram of “drug - active ingredient - target - disease” was made by Cytoscape 3.10 software, and the core target was selected by topological analysis. DAVID database was used for GO and KEGG pathway enrichment analysis, and molecular docking was performed by Discovery Studio software. **Results** A total of 16 active components of *Rhei Radix* et *Rhizoma* were screened, including emodin, β-sitosterol, rhein, emodin methyl ethol, etc., and core targets such as Akt1, MMP9, EGFR, SRC, CASP3 were screened. The signaling pathways of *Rhei Radix* et *Rhizoma* for the treatment of knee arthritis are mainly concentrated in proteoglycan pathway, cancer pathway, endocrine resistance pathway, prostate cancer pathway, epidermal growth factor receptor signaling pathway, focal adhesion pathway, and human giant cell infection pathway. Molecular docking showed that core components emodin, β-sitosterol, rhein, emodin methyl ether and core targets Akt1, MMP9, EGFR, SRC, CASP3, and so on were well docked. **Conclusion** Active components such as emodin and rhein in *Rhei Radix* et *Rhizoma* may regulate multiple signaling pathways by acting on Akt1, MMP9, EGFR and other targets to achieve the therapeutic effect of knee osteoarthritis.

Key words: *Rhei Radix* et *Rhizoma*; knee osteoarthritis; network pharmacology; molecular docking; β-sitosterol; emodin; rhein

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