INPLASY PROTOCOL

To cite: Zhang et al. Effect of shikonin on the proliferation and apoptosis of human ovarian cancer cell SKOV3: a protocol of systematic review and meta-analysis. Inplasy protocol 202040146. doi: 10.37766/inplasy2020.4.0146

Received: 22 April 2020

Published: 22 April 2020

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Support: **SRPHLJHFPC (2018270)**

Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest: **None.**

Effect of shikonin on the proliferation and apoptosis of human ovarian cancer cell SKOV3: a protocol of systematic review and meta-analysis

Zhang, DF[1]; Zhao, DX[2]; Liu, XZ[3]; Li, J[4]; Hu, YH[5]; Dou, PH[6].

Review question / Objective: **Can shikonin effectively manage the proliferation and apoptosis of human ovarian cancer cell SKOV3 (HOCC-SKOV3)?**
Condition being studied: **Shikonin; human ovarian cancer cell SKOV3.**
Information sources: **We will undertake a comprehensive electronic databases search in Cochrane Library, MEDLINE, EMBASE, Scopus, Cumulative Index to Nursing and Allied Health Literature, WANGFANG and China National Knowledge Infrastructure. All electronic databases from the beginning to March 1, 2020 without limitations related to the language and publication status. There is an example for search strategy of Cochrane Library. Similar search strategies for other electronic databases will be built. In addition, we will also search reports on relevant agencies, related conference abstracts, and reference lists of eligible studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 April 2020 and was last updated on 22 April 2020 (registration number INPLASY202040146).

INTRODUCTION

Review question / Objective: **Can shikonin effectively manage the proliferation and apoptosis of human ovarian cancer cell SKOV3 (HOCC-SKOV3)?**

Condition being studied: **Shikonin; human ovarian cancer cell SKOV3.**

METHODS

Participant or population: **This study will choose HOCC-SKOV3 as its research targets.**

Intervention: **Shikonin was used for the management of HOCC-SKOV3 in the experimental group.**

Comparator: There are many alternative management options for HOCC-SKOV3 in the control group. However, studies used shikonin as a control intervention will not be considered.

Study designs to be included: We will include case-controlled studies (CCSs) or randomized controlled studies (RCSs) of shikonin on the proliferation and apoptosis of HOCC-SKOV3.

Eligibility criteria: We will include all case-controlled studies (CCSs) or randomized controlled studies (RCSs) that examine the effects of shikonin on the proliferation and apoptosis of HOCC-SKOV3.

Information sources: We will undertake a comprehensive electronic databases search in Cochrane Library, MEDLINE, EMBASE, Scopus, Cumulative Index to Nursing and Allied Health Literature, WANGFANG and China National Knowledge Infrastructure. All electronic databases from the beginning to March 1, 2020 without limitations related to the language and publication status. There is an example for search strategy of Cochrane Library. Similar search strategies for other electronic databases will be built. In addition, we will also search reports on relevant agencies, related conference abstracts, and reference lists of eligible studies.

Main outcome(s): Primary outcome is proliferation and apoptosis of HOCC-SKOV3. Its proliferation is examined by cell viability test, and its apoptosis is detected by flow cytometry. Secondary outcomes are included HOCC-SKOV3 proliferation and apoptosis related-proteins expression. The proteins comprise of cyclin D1, CDK2, P18, p-Rb, Bcl-2, Bax, cleaved caspase-3, p-PI3K, and p-AKT.

Data management: To extract data from eligible articles, a predefined data extraction sheet will be constructed to make sure all data collected integrity and relevance. Two researchers will independently extract data as follows: publication information (e.g. first author, year of publication, et al), information of HOCC-SKOV3, study design, sample size, study methods, intervention, controls, and follow-up information. Any confusion will be cleared up by discussion with another researcher. If there is insufficient or missing data, we will contact the primary authors by email or telephone.

Quality assessment / Risk of bias analysis: Two researchers will separately appraise study quality of all eligible studies. We will settle any divergence in the evaluation through discussion with a third researcher. We will use Newcastle-Ottawa Scale to assess the study quality for CCSs, and will employ Cochrane risk of bias tool to evaluate study quality for RCSs.

Strategy of data synthesis: This study will use RevMan 5.3 software to implement statistical analyses. We will estimate treatment effects of dichotomous values as risk ratio and 95% confidence intervals (CIs), and continuous values as weighted mean difference or standardized mean difference and 95% CIs. I^2 test is employed to examine heterogeneity across studies. $I^2 \leq 50\%$ indicates homogeneity, and a fixed-effects model will be applied, while $I^2 > 50\%$ exerts significant heterogeneity, and a random-effects model will be placed. We will conduct a subgroup analysis to examine the possible sources of substantial heterogeneity.

Subgroup analysis: A subgroup analysis will be performed to examine the sources of significant heterogeneity according to the different types of studies, study quality, and intervention and comparators.

Sensibility analysis: A sensitivity analysis will be carried out to investigate the stability for study findings by eliminating studies with low methodological quality.

Country(ies) involved: China.

Keywords: Shikonin; human ovarian cancer cell SKOV3; effect.