AJMB AN OPEN ACCESS JOURNAL
eISSN: 2600-8173
https://doi.org/ 10.37231/ajmb.2022.6.S1.579
https://journal.unisza.edu.my/ajmb

PENERBIT Universiti Sultan Zainal Abidin

Asian Journal of Medicine and Biomedicine

The Potential Anti-Osteosarcoma Activity from Naturally Extracted Phenolic Compound: A Scoping Review

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Received: 25th July 2022 **Accepted: 23rd August 2022** **Published: 30th October 2022**

Abstract

Chemotherapy is the standard treatment component for osteosarcoma alongside the surgery. Nevertheless, the survival rate of patients diagnosed with osteosarcoma has not changed over the past three decades. Phenolic compounds are widely reported for having anti-proliferative effects against various cancers including osteosarcoma. Based on the framework published by Arskey and O'Malley [1] this scoping review was conducted to map the published literature on the anti-osteosarcoma activity of the phenolic compounds.

Initially, a literature search was conducted from electronic databases like PubMed, Scopus, EBSCO, Google Scholar Science Direct, and Web of Science. Articles on anti-osteosarcoma activities of phenolic compounds that were published between January 2001 and May 2022 were retrieved. The review process was guided by the framework of systematic reviews and meta-analysis (PRISMA) [2].

In total, 3168 articles were retrieved from the literature search. After a thorough screening, 95 articles were included in the final analysis after met the inclusion criteria. Most of the studies were published between the year 2011 to 2022 (84.2%) and only a few were published between 2001 to 2010 (15.8%) (Table 1). Among the selected studies, 53 types of phenolic compounds were identified to have a promising anti-osteosarcoma activity. Curcumin (12.6%) was the most reported phenolic compound followed by quercetin (11.6%) and resveratrol (10.5%) (Table 2). All studies were utilised *in-vitro* studies (n = 95), and some also conducted *in-vivo* evaluations (n = 17). MG-63 (50.5%) was identified to be the most used cell line. Meanwhile, BALB/c nude mice (58.8%) was the most frequently used in the *in-vivo* evaluation. In this review, it was found that 13 studies analysed the combination between phenolic compounds and chemotherapeutic drugs with 53.8% of the analysis demonstrating synergistic effect.

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Table 1: Summary of the selected studies

Characteristics	Number of studies
Years of publication	
January 2001 – December 2010	15 (15.8%)
January 2011 – May 2022	80 (84.2%)
Experimental types	
In-vitro	95 (100%)
In-vivo	17 (17.9%)
Types of Cell lines (*In-vitro*)	
MG-63	48 (50.5%)
U2OS	46 (48.5%)
SaOS-2	30 (31.6%)
MG-63/DOX, MNNG/HOS, MNNG/HOS-MTX, ROS 17/2.8, HOS-1. K7-M2wt, KHOS, 17/2.8, G-292	1 (1.1%)
Types of Animals (*In-vivo*)	
BALB/c nude mice	10 (58.8%)
BALB/c AnN.Cg*Foxn*^{nu}/CrlNarl mice, (SCID) mice, SCID hairless mice, NOD/SCID mice, nude mice, mice & Wistar rat.	1 (5.9%)

Table 2: Types of phenolic compounds in the selected studies

Phenolic compounds	Number of studies
Curcumin	12 (12.6%)
Quercetin	11 (11.6%)
Resveratrol	10 (10.5%)
Epigallocatechin gallate (EGCG)	7 (7.3%)
Chlorogenic acid, Ellagic acid, Gallic acid	3 (3.2%)
Ascochlorin, Calycosin, Chalcone, Icaritin, Punicalagin, Tannic acid	2 (2.1%)
2,4-Chebulyl-b-D-glucopyranose, 2'-Hydroxyflavanone, 6-Gingerol, Apigenin, Aspidin PB, Baicalein, Biochanin A, Butein, Caffeic acid, Caffeic acid phenethyl ester, Carnosic acid, Carnosol, Carvacrol, Chebulinic acid, Cyanidin 3-O-Glucoside, Daidzein, Delphinidin, Dodecyl gallate, Ferulic acid, Fisetin, Gallic acid, Genistein, Geraniin, Gossypol, Hesperetin, Hyperoside, Licochalcone A, Luteolin acid, Maclurin, Naringenin, Nonylphenol, Oleandrin, Oleocanthal, Oleuropein, Oxyesveratrol Phellamurin, Pterostilbene, Rosmarinic acid, Salidroside, Silibininin, Thymol, Wogonoside	1 (1.1%)

The number of published articles on the anti-osteosarcoma activities of phenolic compounds has increased dramatically over the past 10 years. Phenolic compounds became the main choice in oncotherapy research as it represents a major secondary metabolite in the plant. In this review, all the selected articles utilised *in-vitro* studies, and only several studies conducted *in-vivo* evaluations. For the *in-vitro* study, MG-63 was most frequently used because this cell line was reported to have phenotypic stability [3]. For the *in-vivo* study, BALB/c nude mice was mostly used because the utilization of immunocompromised mice has become an essential tool in the drug evaluation for cancer to maintain the tumour pathological traits [4]. Even though most of the compounds showed a remarkable inhibitory effect *in-vitro* and *in-vivo*, no clinical trial study was reported. Combination analysis is one of the efforts to induce the effectiveness of the treatment. Seven studies reported the synergistic effect when phenolic compound was combined with chemotherapeutic drug. The synergistic effect is the most desired drug-drug interaction in the application of the combination treatment as it can induce treatment efficacy [5].

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In conclusion, this scoping review indicated a significant increase in the evaluation of the anti-osteosarcoma activity of the phenolic compounds. Yet, several research gaps are remaining to be investigated like combination analysis and further continuation of clinical trial study so that the development of phenolic compound-based drugs for osteosarcoma treatment can be realised soon.

Keywords
Anti-osteosarcoma activity, Phenolic compound, Scoping review

Acknowledgment
The authors would like to express a special thanks to the Universiti Sains Malaysia (USM) for providing the fund under the Research University Grant (RUI) (1001/PPSK/8012318).

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