
Antiproliferative and Apoptotic Effects of Ziziphus Extract in Human Breast Cancer Cells

Cancer continues to be and is increasingly a serious health problem and one of the leading causes of death in the world (Saika and Sobue 2013). Breast cancer (BC) is one of the common diseases among women and occupy with cervical cancer the first and the second most common malignancies among women worldwide, respectively (WHO, 2013; Dimitrakopoulos et al., 2015). The occurrence of it around the world is predicted to increase to 2.3 million by 2030 (Twelves and Stebbing 2012). In 2009, about 1.308 new BC cases were reported in the Kingdom of Saudi Arabia (KSA) and it was the ninth leading cause of death for females in 2010 (Lozano et al., 2012; Mokdad et al., 2014). According to Saudi Cancer Registry, BC patient was 25% from all cancer cases registered with expectation for increasing incidence over the coming decades in the KSA which lined with population`s growth and aging (Ibrahim et al., 2008; SCR, 2013, ACS, 2016).

Breast cancer treatment strategies are largely dependent on tumor characteristics including size, extent of spread and cancer cell classification as well as patient preference (Tang et al., 2016). Treatment usually involves surgery, radiation therapy (before or after surgery), chemotherapy, hormonal therapy or targeted therapy. Targeted therapeutic approaches are the induction of apoptosis or inhibition of several processes in the cell such as anti- apoptosis, cell cycle progression, signal transduction and angiogenesis (Schlotter et al., 2008).

Complementary and alternative medicines have been evaluated in addition to chemotherapy, radiation, and surgery in treating cancer. In recent years, researchers draw their attention to the nature compounds included in plants due to their projected low costs, fewer side effects, and low toxicity compared to the standard treatment, the development of new agents such as medicinal herbs with anticancer effects can herald a promising future in cancer treatment (Mans et al., 2000). The practice of application of medicinal plants for relief from many illnesses dates back to ancient times (Sampson, 2005).

Plants contain a diversity of beneficial compounds, including a wide range of phenolic compounds, flavonoids, lignans, and phytosterols. Abundant data indicates that these compounds such as isoflavone and other compounds have an ability to inhibit local estrogen synthesis and induce epigenetic changes (Bilal et al., 2014). According to the most recent studies, phytoestrogens have demonstrated positive effects on BC prognosis, through receptor binding antagonism; it potentially inhibits BC and work synergistically with the chemotherapeutic drugs (Hsieh et al., 2018).

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Many foods and plants in Arabic region have described as phytoestrogens sources including: nuts, oilseeds, soy contents and jujuba plant. The last one (jujuba) has a long history of use for nutrition and the treatment of a broad spectrum of diseases such as human cancers.

Z. jujuba is a herbal plant used in traditional medicine. It can be used for the curing of many kinds of illness including diabetes, diarrhea, skin infections, liver complaints, urinary disorders, obesity, fever, pharyngitis, bronchitis, anemia, insomnia, cancer, and also for blood purification (Li et al., 2007; Ghaly et al., 2008; Pawlowska et al., 2009). The maturity of jujuba fruit may have an influence on both the nutritional and bioactive components and consequently on anticancer activity (Tahergorabi et al., 2015).

The *Z. jujuba* fruit contain different compounds including: triterpenic acids, flavonoids, cerebrosides, phenolic acids, α -tocopherol, β -carotene, and unsaturated fatty acids (Gao et al., 2013). Additionally, it has more total phenolic compounds compared to other common fruits that exhibit antioxidant activities (D'Archivio et al., 2007; Carlsen et al., 2010).

The triterpenic acids, present in the extract, are in the form of free acids or glycones such as saponins, which have multiple biological effects including anti-inflammatory (Fan et al., 2004) anti-microbial (Gbaguidi et al., 2005) hepatoprotective (Tahergorabi et al., 2015), antioxidant effects (Kalogeropoulos et al., 2010) and inhibit of P-glycoprotein (Pgp) in cancer cells (Borska et al., 2012). In recent years, the anticarcinogenic and antitumor activities of triterpenic acids have made them attractive in the fields of scientific research and health care products (Taechakulwanijya et al., 2016; Seca and Pinto 2018). This study aims to investigate the antiproliferation and apoptosis-inducing effects of *Z. jujuba* extracts on human breast cancer cells MCF7 as well as its impact on chemoresistance in vitro.

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