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Journal of Embryology & Stem Cell Research
ISSN: 2640-2637

Potentials of Spices Diet-Derived Polyphenols in Modulating the Self-Renewal of Stem Cells

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Mini Review
Volume 5 Issue 1
Received Date: February 22, 2021
Published Date: March 02, 2021
DOI: 10.23880/jes-16000148

Abstract

Over many centuries, spices have been and are globally utilized in foods and drinks, as well as in pharmaceuticals industries. Spices are rich in health-beneficial chemical constituents that include diet- derived polyphenols, terpenes, polysaccharides, lipids, organic acids, and raw fibres. Stem cells can self- renew and differentiate into major cell types. However, malignant stem cells can invade and kill nearby tissue as well as spread to other body parts through the blood and lymph systems leading to several diseases including cancers affecting the lungs, liver, breasts, pancreas, stomach, colorectum, and cervix. The purpose of this mini-review is to highlight the contributions of recent research on the role of different diet-derived polyphenols from spices mainly cardamom (*Elettaria cardamomum*); cinnamon (*Cinnamomum zeylanicum*); clove (*Syzygium aromaticum*); ginger (*Zingiber officinale*); nutmeg (*Myristica fragrans*); pepper (*Piper nigrum*); saffron (*Crocus sativus*); turmeric (*Curcuma longa*) and vanilla (Vanilla planifolia) in the modulation of the self-renewal of normal and malignant stem cells. Recent researches have demonstrated that predominant compounds; curcumin, crocetin, crocin, gingerols, shogaols, myristicin, piperine, and vanillin possess immunomodulatory effects that specifically inhibit or suppress the proliferation of cancer cells by stimulating the development of normal stem cells, encouraging apoptosis, and activating the expression of protective genes that prevent the formation of malignant cells. More attention should focus on spices and their advanced applications into nutraceuticals for the prevention and management of chronic illnesses. Further work using a combination of in vitro and in vivo methods is needed to fully understand the synergistic impacts of combining more of these compounds to express their modulation effect on the self-renewal of stem cells.

Keywords: Spices; Diet-Derived Polyphenols; Normal Stem Cells; Malignant Stem Cells; Self-Renewal

Introduction

Spices are plants or parts, used for seasoning and impart flavour to foods and drinks. Despite that, the cultivation of spices faces constraints such as disease incidence Shango AJ, [1] but still, they are successfully cultivated in tropical regions due to favourable climatic conditions [2]. Spices are sparingly used due to their strong flavours, but they have also been widely utilized as preservatives and in pharmaceuticals industries globally for many centuries. Spices are rich in diet-derived polyphenols, terpenes, polysaccharides, lipids, organic acids, and raw fibers. Nevertheless, the health benefits of the common and widely used spices are mainly attributed to their diet-derived polyphenols [3]. Various research studies have explored the role of spices on several types of stem cells [4,5]. Stem cells are exceptional human cells that can develop into many different cell types ranging from muscle cells to brain cells, and occasionally fix damaged or lost tissues [6]. Self-renewal is the fundamental property that ensures that the stem cell population is maintained

or does not shrink in size, through numerous cycles of cell growth and cell division (i.e. cell proliferation) with the maintenance of the undifferentiated state [6]. Through the process of self-renewal, stem cells divide to make more stem cells, perpetuating the stem cell pool throughout life.

Often, self-renewal requires cell cycle control and often maintenance of multipotency or pluripotency based on the kind (i.e. normal or malignant) of stem cell [7]. Both normal (embryonic, germinal, and somatic) and malignant (cancer) stem cells can self-renew and differentiate into major cell types within the body parts [8]. Malignant cells can invade and kill nearby tissue and spread to other body parts through the blood and lymph systems. There are several diseases in which malignant cells divide without control and can invade nearby tissues [7]. These diseases include carcinoma; sarcoma; leukemia; lymphoma and melanoma as well as cancers that affect the breasts, lungs, colorectum, kidney, bladder, liver, stomach, cervix, and the central nervous system particularly in the tissues of the brain and spinal cord. Research has revealed that modulation of the self-renewal of stem cells by dietary-derived polyphenols is significant to potentially manage and prevent diseases [6,9,10]. The purpose of this mini-review is to highlight the contributions of recent research on the role of different spice diet-derived polyphenols in the modulation of the self-renewal of stem cells.

Cinnamic Acid

The study by Huang, et al. [11] revealed that cinnamic acid, obtained from cinnamon (*Cinnamomum zeylanicum*) can impede proliferation, encourages apoptosis, promotes differentiation, reduces the invasive ability of lung cancer stem cells, and increases their sensitivity toward cisplatin and paclitaxel.

Curcumin

Curcumin (CUR) an effective polyphenol extracted from the rhizome of turmeric (*Curcuma longa*) has been explored as an anticancer agent. CUR restricts breast stem cell self-renewal, while it is safe/non-toxic to normal/differentiated cells [12]. CUR inhibits the signaling pathways, which play key roles in cancer development and progression. Also, inhibition of Sp-1 and its housekeeping gene expressions may serve as an important hypothesis to prevent cancer formation, migration, and invasion.

Ginger Oleoresin

The ginger oleoresin is a semi-solid extract, composed of resin and essential or fatty oil obtained by ethanol or acetone extraction from the dried and unpeeled rhizome of ginger (*Zingiber officinale*). It is rich in gingerols, shogaols, and their derivatives which induce the self-renewal of stem cells which activate the expression of protective genes that prevent the formation of malignant cells [13].

Myristicin

Myristicin is an allylbenzene in nature and is a chief active constituent in nutmeg (*Myristica fragrans*). The widespread consumption of nutmeg and its essential oils through food, drinks, or medicines has exposed humans to myristicin. This polyphenol modulates gene expression in human leukemia cells and induces apoptosis [14]. A more recent study by Mickus, et al. [15] showed that, at higher doses, nutmeg essential oils are capable of reducing the viability, proliferation, and colony formation of malignant cells.

Piperine

Piperine, an alkaloid isolated from pepper (*Piper nigrum*), has an effect on progenitor cell proliferation and enhances the effect on breast stem cell self-renewal by exhibiting effects on mammosphere size and colony formation [16]. A study by Lu, et al. [17] showed that piperine inhibits breast stem cell self-renewal and does not cause toxicity to normal/differentiated cells, this is achieved by the differentiation of stem cells which induces apoptosis.

Crocetin and Crocin

The purified crocetinic acid from saffron (*Crocus sativus*), inhibits the proliferation of pancreatic cancer cell lines in a dose and time-dependent manner as well as inducing apoptosis [18,19], and it suppresses the growth of tumor [18]. Furthermore, the use of crocetin and crocin induces stem cell differentiation which in-turn inhibits the proliferation of malignant cells [20]. Milajerdi, et al. [19] reported that crocin increases apoptosis in malignant cells by inhibiting the synthesis of Ribonucleic acid (RNA) and Deoxyribonucleic acid (DNA) of the cancer cells. While crocetin inhibits the growth of cancer cells by reducing the synthesis of DNA, RNA, and protein in neoplastic cells, RNA polymerase II inhibition, and interaction with histone H1 and H1-DNA structures [5,19].

Vanillin

Vanillin, a natural compound from vanilla (*Vanilla planifolia*) cured beans, exhibited protective effects by inducing stem cell differentiation which significantly suppresses the growth of malignant cells [21,22]. Srinual, et al. [23] investigated the effect of vanillin on anchorage-independent growth and the motility of human non-small

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cell lung cancer cells and found that vanillin suppresses cancer cell growth

Synergistic Effects on Stem Cells

Breast stem cell self-renewal can be inhibited by the consumption of both curcumin and piperine separately, and in combination, and they do not cause toxicity to the normal/differentiated cells. The study by Kakarala, et al. [16] showed that both curcumin and piperine inhibit the formation of malignant breast cancer cells and there was no effect on cellular differentiation. Therefore, the compounds could be potential cancer preventive agents. Xie, et al. [4] reported that food-derived compounds with low toxicity such as the piperine and dimeric amide alkaloids (*chabamide*, *chabamide I, nigramide B, piperolactam A and piperolactam* B) isolated from the 60% methanol-soluble fraction of the ethanol extract of the P. nigrum stems, can be used as sensitizers to overcome paclitaxel resistance in human cervical cancer or cervical carcinoma. The same study showed that combination treatment enhanced cell apoptosis. Fluorescent magnetic submicronic polymer nanoparticles (FMSP-nanoparticles) and clove (*Syzygium aromaticum*) extract exhibited anticancer properties, nevertheless, it has been shown that sole treatment does not elicit a significant response on human breast cancer cells [24].

Conclusion

Spices play a significant role in modulating the self-renewal of stem cells, either solely or in combination. Spices can inhibit or suppress the proliferation of cancer cells by stimulating the development of normal stem cells, encouraging apoptosis, and activating the expression of protective genes that prevent the formation of malignant cells. However, more attention should focus on spices and their advanced applications into nutraceuticals for the prevention and management of chronic illnesses. Further work using a combination of in vitro and in vivo methods is needed to fully understand the synergistic impacts of combining more of these polyphenols to express their modulation effect on the self- renewal of stem cells.

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