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Mobilization of Stem Cells Using Plant Extracts

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ABSTRACT

Stem cell therapy is an emerging therapeutic in clinical therapy which has ability to self-renew and differentiate cells into different cell lineages. Various biological and semi-synthetic components are using as stimulants for mobilization and differentiation of stem cells. Continuous usage of these stimulants may lead to toxicity, adverse side effects, and high cost effective. To overcome this plant based derived products are using as an alternative source as stimulants in the stem cell therapy for proliferation, mobilization and differentiation of stem cells.

Keywords

Stem cells, Growth factors, Cytokines, Stimulants, Plant extracts.

Introduction

Stem cell therapy is a promising therapeutic technique at the forefront of regenerative medicine. The goal of the stem cell therapy is to regenerate and repair on damaged or injured tissues in the body [1]. Stem cells have the ability to self –renew and differentiate into mature cell lineages. Human mesenchymal cells (hMSCs) are multi potent group of cells first described by Friedenstein in 1970s. MSCs are population of cells derived from bone marrow, adipose tissue, umbilical cord and placenta [2]. These cells have ability to differentiate into wide variety of cell lineages osteoblasts, adipocytes, chondrocytes, tenocytes and myocytes.

MSCs have also capacity to exhibit immunomodulatory and immunological tolerance inducing characteristics [3-9]. For proliferation and differentiation of stem cells cytokines and growth factors were used in stem cell therapy.

Growth factors and cytokines are produced by mesenchymal stem cells which are suitable for inducing endogenous repair of damaged tissue. These growth factors and cytokines will help in the proliferation, differentiation, mobilization and homing of stem cells. Components isolated from human biological sources were used for stem cell production previously but due to ethical issues now recombinant and synthetic components are using as an alternative stategy [10]. Various semi biological and synthetic substances are currently used as stimulants for the proliferation and differentiation of stem cells. For example, in vitro osteogenic differentiation is by means of adding mixture of dexamaethasone, ascorbic acid and β-glycerophosphate were used as a stimulant. Mobilization and differentiation of murine cells into cardiomycetes is by means of cytokine- granulocyte stimulating factor (G-CSF), growth factors like vascular endothelial growth factor, stromal cell derived factor (SDF1/CXCL12) and SDF-1 receptor CXCR4.

Limitations

Even though, semi biological and synthetic components are using as stimulants because of their cost effective, toxicity and side effects has led to researchers globally for alternative search for these stimulants. In osteogenic differentiation, continous usage of ascorbic acid at 37 °C is highly unstable and toxic at high doses [11]. Dexamethasone, a cock tail factor in the osteogenic differentiation is an immune suppressor and may lead to cause malignant formation sometimes [12,13]. Glucocorticoids administration for long term has shown undesired side effects including immunosuppression and other severe bone loss and increased risk of fracture [14-16].

Because of its limitations and side effects, natural products i.e., plant based derived products and plant extracts emerged as an alternative source for the growth stimulants in proliferation and differentiation of stem cells. The research with the plant based derived products have been well established. Anti-diabetic, anti-hypertensive, antimicrobial, anti-inflammatory, anti-adipogenic effects from the plant based products have been proved. Main advantage in the usage of plant based products is its availability,

affordability and low toxicity. The world health organization (WHO) has recognized the potential ability of traditional remedies and strives to preserve the primary health care.

Role of plant base products in the stem cell therapy

Plant extracts contains bioactive ingredients in the form of secondary metabolites or phytochemicals such as phenols, polyphenols, flavonoids, tannins, alkaloids, and glycosides etc., Indian traditional plant based medicine, AYURVEDA and Chinese traditional medicine has been used for the treatment of ailments since ages [14]. Single active ingredient and also mixture of plant crude extracts (poly herbal formulations) have effect in showing promising results in traditional medicine. Terminalia bellerica, which contains high amount of gallic acid, can be used as a scaffold model with hydrogel composition for use in stem cell therapy. Some of the plant based extracts used in the differentiation of stem cells are tabulated in the table.

Herbal extract	Effect	Mechanism of action
Chinese herbal extract (ZD-1)	Osteogenic effect	Proliferation and inhibitory effects on mineralization of hMSCs through down regulation of osteocalcin. BMP-2 and osteopontin [17]
Drynariae fortune	Osteogenic effect	Regulation of β-catenin via AKt and AMPK signalling [18]
Ligusstrum lucidum	Osteogenic	Increased expression of osteogenesis stimulating genes (β-catenin, BMP-2, cyclin D1, MT1MMP,osteoprotegerin and TBX3T [19]
Dipasacus asper	Osteogenic	Induced alkaline phosphatase activity and expression of bone specific proteins (Sialoprotein and Osteocalcin) [14]
Foeniculum vulgare	Osteogenic	Estrogenic activity [20]
Olive leaf extract	Angiogenesis	Increased expression of vascular endothelial growth factor, PCAM, platelet derived growth factor, VEGFR-1 [21]
Curcuma longa	Angiogenesis	Enhances proliferation of AD-hMSCs into endothelial progenitor cells through increased expression of CD34, CD133 and VEGFR2 [22]
Dhanawantra kashaya	Nerve regeneration	Increased proliferation and delayed senescence of wharton's jelly derived-hMSCs [23]
Carica papaya	Thrombocyte increased action	Regulates in vitro synthesis of thrombopoiesis

Table 1: The following table summarizes the list of plant extracts stimulates mesenchymal stem cells resulting in proliferation and differentiation. *(Source –The present data was adopted from the Udalamaththa et al., 2016 [24] published in Stem cell Research & Therapy and tabulated).*

Limitations and draw backs of herbal extracts

Usage of herbal extracts in the stem cell therapy has also de limits and drawbacks. Plant based products exhibited promising results in in vitro but application of these products in the stem cell therapy requires more in better understanding the mechanism of action and effective pathways. Clinical applications are challenging because of variability and complexity of secondary metabolites, other factors like environment and genetic are also limitations in the usage of herbal extracts.

Conclusion

Stem cell therapy emerged as potential therapeutic application in regenerative medicine. Usage of plant based products in the stem cell therapy as stimulants replacing cytokines and growth factors needs to study further deeply in better understanding the mechanism of action and pathways.

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