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Review

Aglycone solanidine and solasodine derivatives: A natural approach towards cancer

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ABSTRACT

Over the past few years, it was suggested that a rational approach to treat cancer in clinical settings requires a multipronged approach that augments improvement in systemic efficiency along with modification in cellular phenotype leads to more efficient cell death response. Recently, the combinatory delivery of traditional chemotherapeutic drugs with natural compounds proved to be astonishing to deal with a variety of cancers, especially that are resistant to chemotherapeutic drugs. The natural compounds not only synergize the effects of chemotherapeutics but also minimize drug associated systemic toxicity. In this review, our primary focus was on antitumor effects of natural compounds. Previously, the drugs from natural sources are highly precise and safer than drugs of synthetic origins. Many natural compounds exhibit anti-cancer potentials by inducing apoptosis in different tumor models, in-vitro and in-vivo. Furthermore, natural compounds are also found equally useful in chemotherapeutic drug resistant tumors. Moreover, these Phyto-compounds also possess numerous other pharmacological properties such as antifungal, antimicrobial, antiprotozoal, and hepatoprotection. Aglycone solasodine and solanidine derivatives are the utmost important steroidal glycoalkaloids that are present in various Solanum species, are discussed here. These natural compounds are highly cytotoxic against different tumor cell lines. As the molecular weight is concerned; these are smaller molecular weight chemotherapeutic agents that induce cell death response by initiating apoptosis through both extrinsic and intrinsic pathways.

Contents

1. Introduction . . . 447
2. Steroidal alkaloids/Glycoalkaloids . . . 448
3. Aglycone solanidine alkaloids . . . 448
   3.1. Solanine . . . 448
      3.1.1. Toxic effects of solanine . . . 448
      3.1.2. Antitumor effects of solanine . . . 448
   3.2. Chaconine . . . 449
      3.2.1. Anticancer activity of chaconine . . . 449
      3.2.2. Antimetastasis of chaconine . . . 450
4. Aglycone solasodine alkaloids . . . 450
   4.1. Solamargine . . . 450
      4.1.1. Anticancer effect of solamargine . . . 450
      4.1.2. Cytotoxicity in human hepatic cell line . . . 452

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4.1.3. The activity of solamargine against breast cell carcinoma . . . 452
4.2. Solasonine . . . 453
5. Solasodine rhamnose glycoside (SRGs) . . . 453
6. Conclusion . . . 454
7. Future directions . . . 454
Authors contribution . . . 455
Conflict of interest . . . 455
Acknowledgement . . . 455
References . . . 455

1. Introduction

Recently, Cancer is a principal cause of death [1], associated with the development of solid masses known as tumors. In clinics, the management of cancer includes chemotherapy, radiotherapy and surgical removal of tumor masses. In chemotherapy, low-molecular-weight cytotoxic agents are used to be administered. Unfortunately, these cytotoxic agents kill not only the tumor cells but also the healthy cells which result in hair loss, bone marrow suppression, nausea and gastrointestinal tract lesion [2].

Previously, the majority of chemotherapeutic drugs showed cell death response through the induction of programmed cell death (Apoptosis) [3], however; apoptosis is not the only mean to kill and eradicate cancer cells [4,5]. Apoptosis can characterize by cell shrinkage, dilatation of endoplasmic reticulum, DNA fragmentation, chromatin condensation and the formation of apoptotic bodies [6,7] by extrinsic and intrinsic pathway or both. The extrinsic pathway (receptor mediated pathway) results in the activation of cell surface ligand death receptors such as TNFR, Fas and TRAIL receptors while the intrinsic (mitochondrial mediated pathway) pathway associated with the release of cytochrome-C into the cytoplasm, following the mitochondrial disruption and initiate caspase cascade by converting procaspase-9 to caspase-9 and caspase-9 further activate caspase-3 that cause irreversible cell death (apoptosis) [8] (Fig. 1).

Previously, many Phytocompounds and their synthetic and semi-synthetic derivatives are the potential sources of cytotoxic agents [9]. Furthermore, clinical trials for new chemical entities (NCE) or drugs for assessment of their anticancer potentials; about 50% of these come from natural origin [10]. *Solanum nigrum* is a versatile member of Solanaceae family [11] and predominantly breeds in temperate climate region [12]. It is an annual branching herb having dull dark green leaves and small white flowers [13]. At maturation, the berries or fruits of this plant are small in size, black in color and globular in shape [14]. Traditionally, grinded leaves of young plant applied externally for the treatment of sores, carbuncles, swelling and injuries [15]. It has diuretic and antipyretic effect and exploits in the management of edema, inflammation [12] and mastitis [16]. It also used to treat stomach ache, jaundice, liver problems, toothache and many skin diseases [17]. In China and Japan, the entire plant was used in different types of cancer [18] such as liver [12], lungs, urinary bladder, larynx, and carcinoma of vocal cords [19]. Plant also illustrates a number of other pharmacological actions such as;

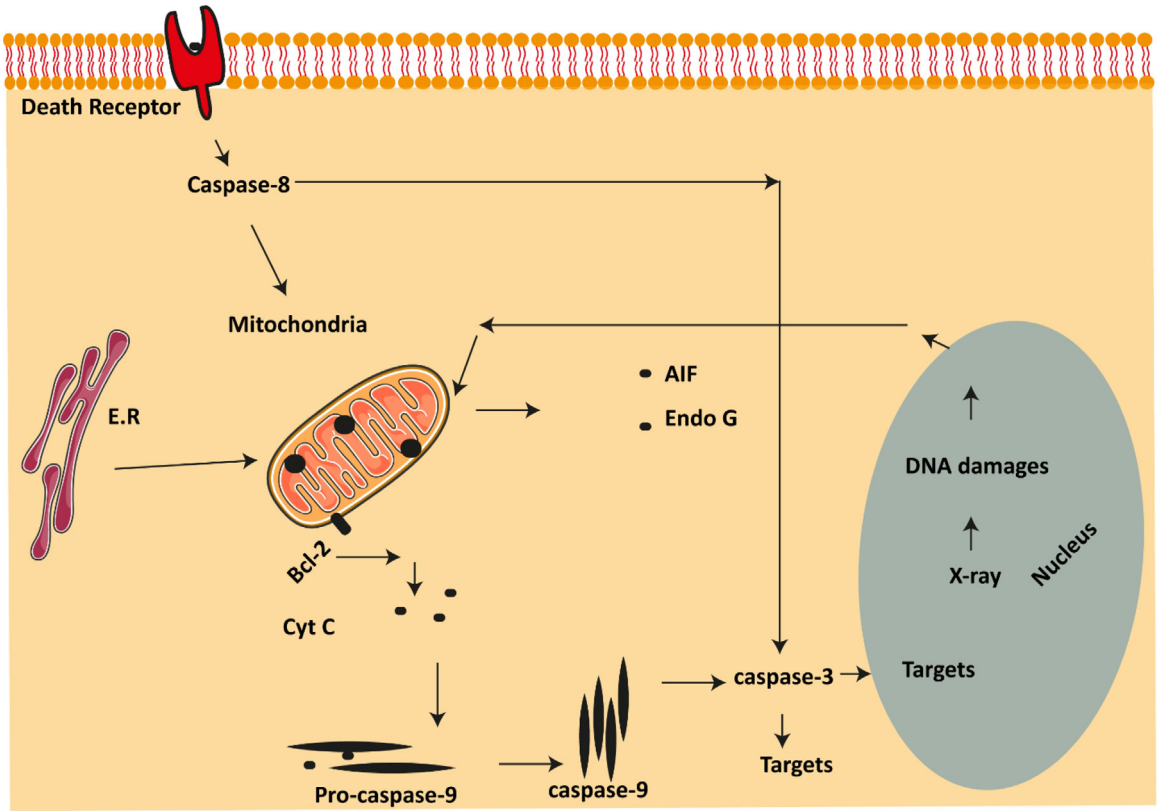

Fig. 1. Apoptosis; intrinsic i.e mitochondrial-mediated pathway and extrinsic or death receptor-mediated pathways [106].