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Ginseng phytochemicals as therapeutics in oncology: Recent perspectives

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ABSTRACT

During the last few decades, cancer has mushroomed as a major health issue; and almost all drugs used for its therapy are very toxic with lethal side effects. Complementary and alternative medicines gain popularity among health professionals in recent era owing to its preventive mechanism against side effect chemotherapeutic drugs. Efforts are focused by scientists to isolate compounds from medicinal plant that have chemotherapeutic attributes; and ability to neutralize the side effects of chemotherapy. Ginseng is an oriental medicinal recipe from Araliceae family and Panax species. The chemotherapeutic effect of ginsenoside is resultant of its appetites, antiproliferative, anti-angiogenic, anti-inflammatory and anti-oxidant properties. The anticancer effect of ginseng is proven in various types of cancer, including; breast, lung, liver, colon and skin cancer. It increases the mitochondrial accumulation of apoptosis protein and downregulate the expression of anti-apoptotic protein. It also aids in the reduction of alopecia, fatigue and nausea, the known side effects of chemotherapeutic drugs. The aim of the present review is to provide the brief review of the recent researches related to mechanism of action of ginseng in different types of cancer as complementary and alternative medicine on different body organs.

1. Introduction

Cancer is a disease which involves abnormal growth of cells with the potential to proliferate and spread into the surrounding tissues. It is a genetic disease which can be inherited by parents or by deoxyribonucleic acid mutation by certain carcinogenic substance e.g., tobacco smoke, pesticide residue; and ultraviolet rays from sun [1]. Human body is constituted of variety of cells; where epithelial cell constitutes 70% of total number of body cell. Epithelial cells are among those which are majorly affected by cancer owing to malignant progression. The tumor cell can be proliferated to the surrounding tissues by mean of lymph nodes, organ and body tissue and called as metastasis. The metastasis occurs in cancerous cell due to downregulating of tumor suppressor gene i.e. P53 [2]. According to global burden of cancer study, 14.1 million new cases and 8.2 million mortality occurred due to cancer throughout the world in 2012 [3].

Complementary and Alternative Medicine (CAM) is termed as a healthcare practice, products, and therapies that are typically not - part of conventional medicine e.g., acupuncture, dietary supplements, massage therapy, and yoga. These are used with or without standard medical care [4]. In clinical practice, dietician can help oncology patient to the effective use of CAM products to prevent the chemotherapeutic effects [5]. From last few years, CAM gain popularity in tumor patient due to enhancement in body immunity against cancer or improvement in physical and mental health [6]. In industrialized countries, 25–50% people used CAM [7]. Chemo preventive effect of CAM may be the resultant of its apoptotic, anti-proliferative, anti-angiogenic, anti-inflammatory and antioxidant properties. Ginseng ability to kill tumor cell and relative nanotoxicity to normal cell make it attractive candidate for used as CAM product. There is no recent review available on the ginseng role on organ specified anti-cancer property. So, purpose of this review is to provide recent knowledge related to the anti-cancer activity of ginseng on different body organs i.e., breast, colon, liver, lung and skin.

2. Composition of ginseng

Ginseng usage in oriental medicinal recipes is thousands years old; but majority of the people standpoint that ginseng cultivation started around three hundred years ago [8]. There are many kinds of ginseng in

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the world, and all are belonged to the *Araliaceae* family in the *Panax* species. The name *Panax* originates from the Greek words means all-healing whilst ginseng comes from Chinese word "*Jen Sheng*" means man-root. The faith is established that ginseng can be beneficial for all aspects of the human body due to the humanoid shape of the root and rhizome of plant [9]. Many species of ginseng are used all over the world, but two most common used species are *Panax ginseng* (Chinese ginseng) and *Panax quinquefolius* (American ginseng). Ginseng is also classified according to their preparation method into fresh ginseng (sliced and eaten without any treatment), white ginseng (dried after peeling) and red ginseng (dried after steaming) [10].

Ginseng used as herbal medicine in the Eastern Asia, especially in Korea and China. A case control study was conducted in South Korea which included 4587 individuals, aged 39 years and older from 1987 to 1991. The result showed that the incidence of death among ginseng user is 60% less as compared to non-ginseng user [11]. Another clinical study was performed in Korea from 1987 to 1992 that shows ginseng user have reduced relative risk (0.40) in comparison to non-ginseng user (0.28) [12]. A case-control study was conducted in Korean Cancer Control Hospital on 1987 pairs, which told that the ginseng help to reduce the risk of cancer among ginseng consumer as compared to non-consumer [13].

The meta-analysis of different research studies shown that ginseng use might be linked with the lower risk of cancer. In a study, the result of reduced cancer risk by ginseng consumption in China had no significant inverse relationship in comparison to Korea. The effect of ginseng as a reduced cancer risk factor is only confirmed in Korea, China and United State. The difference in ecology and population distribution, we cannot manipulate the result from rest of the world. There is need of other study to verify its impact in other countries [14]. In December 1997–December 2008, a randomized, double-blinded, placebo-controlled trial were conducted in four hospitals of Zhejiang Province, China which included 643 chronic atrophic gastritis patients and divided randomly into two groups; Placebo and treatment group. All patient in treatment group take 1g of ginseng extract powder orally in every week for three years and to figure out the impact, the patients were followed up for 8 years. During the study, 16 cases of different type of cancer were diagnosed in placebo group while 8 in treatment group. The treatment group decreased the risk of cancer development (RR = 0.54) in comparison to the placebo group, which has non-significant difference as p value was 0.13 [15].

The pharmacological active ingredient is present throughout the ginseng plant. The main anti-cancer ingredient in ginseng is ginsenoside, which mainly present in root. The root content of ginseng is highly regarded which makes ginseng one of the most expensive and popular herb all over the world [16]. Ginseng root is recognized as king or lord of herb. The three key ingredients of ginseng are saponins, polysaccharides and phenolic compounds [17].

2.1. Saponins

Saponins are main components of ginseng and are recognized as primary pharmacologically active components; ginsenosides is alternative name for saponins [18]. Ginsenoside from ginseng are categorized into two different groups; based on their chemical structure known as oleanane type (five ring structure) and dammarane type (four ring structure). The dammarane type ginsenoside are the major components of ginseng which can be further categorized into two groups based on aglycone bond i.e. 20(S) protopanaxatriol (Re, Rg1, Rh1 and Rg2) and 20(S) protopanaxadiol (Rg3, Rd, Rb3, Rc, Rb1, Rb2). There are 50 types of ginsenosides, separated from the roots of ginseng plant [19]. The oleanane type ginsenoside are anabolic compound of B-amyrin, which are found rarely in ginseng e.g., Ro that is acidic in nature. Many new ginsenoside named as 25-OH-PPD and 25-OH-PPT were recently separated from ginseng berries [20].

2.2. Polysaccharides

Ginseng have two type of polysaccharides, one of them is composed of starch like glucan known as neutral polysaccharide and other is acidic polysaccharide [21]. Acidic polysaccharide have more anti-tumor and anti-oxidant property as compared to neutral polysaccharides [22]. *Panax ginseng* have immunomodulating glycans, ginsenan PB and ginsenan PA [23]. Korean ginseng root extract have panaxans (M, N, O, P, I, J, K, L, A, B, C, D and E) [24].The red ginseng has 7.5% polysaccharide which is three times higher to the white ginseng (0.63%) due to degradation of sugar molecule in the process of preparation of red ginseng by steaming and drying white ginseng [25]. According to Rapp, Pater, Willan, Cormier, Murray, Evans, Hodson, Clark, Feld and Arnold [26] the acidic polysaccharide of ginseng produced nitric oxide (NO) without changing morphology of RAW264.7 macrophage cells. The production of NO in RAW26.7 cell is due to the upregulation of nuclear transcription factor (Ap-1, ATF-2, STAT-1, CREB and Nf-kB).

2.3. Polyacetylene

The ginseng also contains non-water soluble polyacetylene compound. Takahashi and Yoshikura [27] initially isolated the panoxynol polyacetylene compound from ginseng [28]. The polyacetylenes of ginseng does show effect against cancerous cell but in vivo there is no proven fact present owing to their wobbly chemical nature [19]. Most recently researches demonstrate that ginseng acts as a chemo preventive agent owing to its anti-cancer and anti-oxidant properties. In future, ginseng has potential to be used as chemo preventive agent due to its properties related to apoptosis and anti-proliferative mechanism against cancer.

3. Ginseng role in chemotherapy

It is well established fact that chemotherapy has many side-effects, which impacts the patient's quality of life [29]. Ginseng has the magic to minimize the side effects of chemotherapy including; hair-loss, nausea, fatigue and if exercised in combination with other chemo drugs it leads to augmented anticancer activity. A clinical trial was conducted in BenQ Hospital of China. In which 96 patients of Non-Small Cell Lung Carcinoma (NSCLC) were added from January 2013–January 2016. These were distributed randomly in two groups, each group have 48 patients with average age of 32–66 years. The same foundation treatment was given to both groups. The control received dendritic cell (DC) and treatment group received Ginseng Polysaccharides (GPS) with dendritic cell under thoracoscope. The Functional Assessment of Cancer Treatment- Lung ((FACT-L)) was measured to access the quality of life. The (FACT-L) score was decreased in both groups but control group had higher value as compared to the treatment group. The Serum interferon-γ (INF-γ), interleukin-4 (IL-4), IL-2 and IL-5 were measured in both groups before and after treatments. The expression of Th1 cytokines (IL-2, INF-γ) and the ration of the Th1/Th2 cytokines (INF-γ/IL-4, IL-2/ IL-5) is increased and expression of Th2 (IL-4, IL-5) decreased significantly during foundation treatment. When treated with DC and GPS, the treatment group had higher value of Th1 and ratio of Th1/Th2 and lower value of Th2 as compared to the control group. The result showed the GPS with DC have synergic effect on NSCLC patients [30].

Ginseng helps to boost the antitumor effect of epirubicin and paclitaxel drugs by increasing the mitochondrial accumulation of Bax and Bak that mediate cell death by apoptosis. Alopecia is one of the major stressful and negative psychological effect on patient undergoing chemotherapy [31]. It is reported that Korean red ginseng (KRG) helps to promote the hair growth [32]. Cyclophosphamide is a chemo preventive drug which formed metabolite 4-hydroxycyclophosphamide (4-HC) by liver cytochrome P450 (CYP) enzyme and exhibited an anticancer effect [33]. 4-HC clogged human hair growth by enhancing

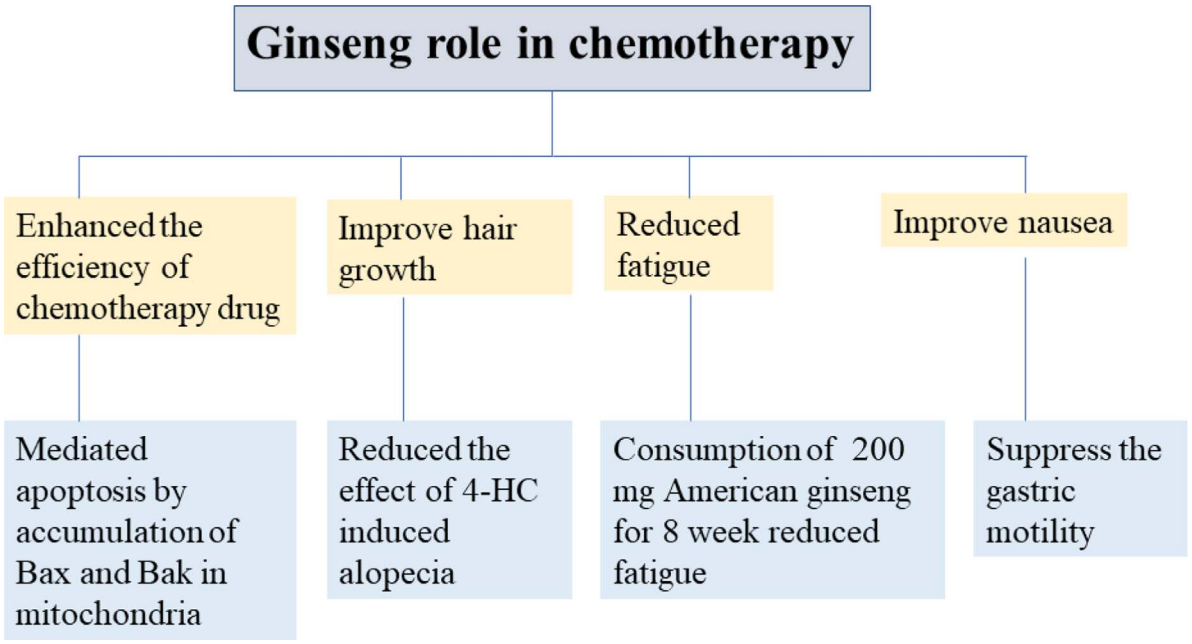

Fig. 1. Ginseng act as chemo sensitizer drug via mediated apoptosis, reduce the alopecia effect of chemo drug, suppress the gastric motility and minimized the fatigue [34,36,37].

apoptosis of hair matrix keratinocytes and cause premature catagen development. KRG may help to prevent against 4-HC-induced alopecia [34]. Ginsenoside in the ginseng has strong affinity to combine with anti-apoptotic protein. It can decrease the activity of anti-apoptotic protein (BCL-2, BCL-XL, and MCL) and induced apoptosis mechanisms in the cancer cell of the human body [35]. Chemotherapy cause weakness and chronic fatigue to the patient and ginseng helps to improve the symptom of fatigue by oral administration. In a study, 2000 mg American ginseng extract was given to cancer patients for eight weeks and change was measured by MFSI-SF (multi-dimensional fatigue symptom inventory short form). Ginseng depicted a much greater impact in active cancer group as compared to study subjects who had completed the treatment process [36]. Cisplatin, another chemotherapy drug causes nausea in patients; red ginseng saponin and non-soponin fractions promoted the suppression of the gastric motility in cancer patients who were on this drug [37]. Ginseng role in chemotherapy management is depicted in Fig. 1.

3.1. Ginseng and breast cancer

Breast cancer is a major health risk for women. Annually, one million women are spotted with breast cancer [38]. Only in Unites States, it is considered as the most prevalent cancer and second important reason of mortality [39]. In 2017, 15% new cases of breast cancer are diagnosed in female and 6.8% of all cancer death is due to the breast cancer. Approximately 12.4% woman are at the risk of the breast cancer [40]. Many interventional studies have been conducted which concluded that ginseng has antitumor effect [41–43]. A case-control clinical study was conducted in 1987. In which 174 cases and 482 controls of breast cancer were included. The odd ratio (0.63) of ginseng dose respond relationship was confirmed the antitumor activity of ginseng [12].

The effect of ginseng on breast cancer is also confirmed by different in vitro studies. Black ginseng (Panax ginseng Meyer) produced by repeated steaming of red ginseng roots, has main component i.e. Rg5, which exhibits anti-tumor effect by stimulating cell death in breast cancer cell (MCF-7) through activation of Mitogen Activated Protein Kinase (MAPK) pathway. Rg5 plays pivotal role as natural ingredient in the prevention of cancer through inhibition of cancer cell proliferation by up regulating the tumor suppressor gene ($p15^{INK4B}$, p53 and $p21^{WAF1/CIP1}$) [42]. Furthermore, ginsenoside-Rg5 inhibits the proliferation of BT-474 and T-47D breast cancer cells to 27.7 and 23.5%, receptively at 10 mg/mL concentration after 48 h exposure through promotion of protein involved in the Adenosine Monophosphate Activated Protein Kinase (AMPK) pathway [43]. Ginsenoside Rg3 from ginseng was also induced the death, impede the growth and metastasis and angiogenesis in carcinoma cell via inhibition of intracellular Ca^{2+} Channel. Additionally, it decreased the multi-drug resistance of tumor cells resulted in improvement of immunity, life quality and increase of life span [44]. In another study, it is concluded that Rg3 halt the propagation and causes death of Human breast cancer cells (MDA-MB-231) by blocking NF-κb signaling and also reduced its transcriptional activity. When MDA-MB-231 cell were treated with Rg3 for 24 h, it significantly stopped the activation of ERK via phosphorylation but level of ERK remained unchanged. After 12 h treatment of Rg3 on MDA-MB-231, the Akt phosphorylation level were also significantly reduced which is directly related to apoptosis. The treatment of Rg3 to MDA-MB-231 can downregulate the expression of p53 mutant depending on concentration of Rg3 and time of treatment by increasing the interaction between p53 and its negative regulator Mdm2 [45]. Anti-apoptotic protein, proliferate the cancer in the body by stopping the apoptosis mechanisms. Ginseng has ginsenosides named as R_f, Rg1, Rg3 and Rh2 which bind with anti-apoptotic protein and induce apoptosis in cancer cell by downregulate the reaction of them. So, ginseng can be used as drug for chemotherapy in cancer patient [35]. In a recent study, Triple Negative Breast Cancer (TNBC) cell lines (BT-549, MDA-MB-231 and MDA-MB-453) cytotoxicity through paclitaxel is promoted by ginsenoside Rg3. The paclitaxel with ginsenoside Rg3 halt the activation of NF- Kb, down regulate the expression of antiapoptotic protein i.e. Bcl-2 protein and p65; and induced apoptosis via increased Bax and capase-3 protein expression [41]. It is further added that ginseng halt the growth of cells in MCF-7 cell line and stopped the 99.2% of cell growth in MDAMB-23T. It has anti-proliferative effect in MCF-7 and MDA-MB-23T cell lines. Ginsenoside Re and Rg2 induced death in MCF-7 breast cancer cell line through arresting the cell cycle by controlling the expression of cyclin A and Cyclin D1 [46]. Anti-cancer action of ginseng on breast cancer is shown in Fig. 2.

Mai, Moon, Song, Viet, Van Phuc, Lee, Yi, Cho and Cho [47] suggested that Ginseng has Ginsenoside F2, which has anti-proliferative activity against breast stem cancer cell and induce apoptosis in breast

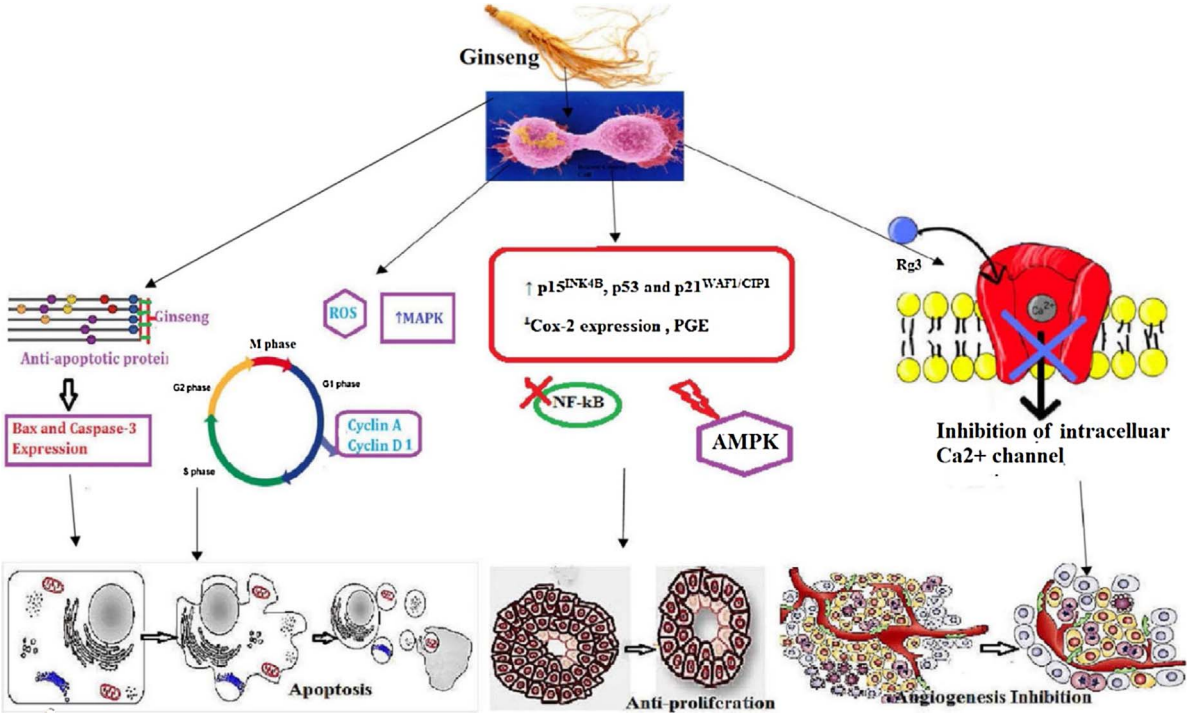

Fig. 2. Ginsenoside Rf, Rg1, Rg3, Rh2 attached to anti-apoptotic protein and control its mechanisms, Ginsenoside Rg3 increase the expression of apoptotic protein Bax and caspase-3. Rg5 upregulate the MAPK pathway. Ginseng compound K produce reactive oxygen species, Ginsenoside Re and Rg2 arrest the cell cycle by controlling the expression of cyclin A and Cyclin D1 that all result in apoptosis. Ginsenoside Rg3 blocked NF-κb signaling and up regulate the tumor suppressor gene (p15INK4B, p53 and p21WAF1/CIP1), Ginseng compound F2 upregulate the p53 gene, ginseng compound K down regulating the Cox-2 expression, lowering the prostaglandin E2 (PGE) level and modulate of AMPK pathway that all impede the proliferation in breast cancer cell. Ginsenoside Rg3 halt the angiogenesis in carcinoma cell via inhibition of intracellular Ca2+ Channel.

stem cancer cell by up-regulation of tumor suppressor gene P53. Ginseng metabolite compound K stopped the growth MCF-7 cell line at 48 h with different concentration levels (10–50 μg/mL). The IC_{50} was 35 μg/mL but compound K did not show any cytotoxicity in MCF-10A (human normal breast cancer cell line) as compared to MCF-7 cell line. In this study, compound K stopped the cell proliferation and induced apoptosis in MCF-7 cells via production of reactive oxygen species and down regulating the Cox-2 expression and lowering the prostaglandin E2 (PGE) level by modulation of AMPK pathway [48]. The ginseng compound K (CK) was given with or without cisplatin (DDP) to MCF-7 cell line of breast cancer to measure its tumor inhibition. This study included 4 groups; control, CK, DDP, CK + DDP treatment was given, respectively. The tumor inhibition result showed that after 48 h application of CK, DDP and CK + DDP to MCF-7 cell line, the inhibition rates were, 9.18 ± 2.25, 21.34 ± 2.84, and 43.37 ± 5.62, respectively. The ginseng compound K with DDP significantly reduced the tumor as compared to CK and DDP separate group. The apoptosis in all treatment group was significantly increased ($p < 0.05$) as compared to the control group. The apoptosis rates were 3.14 ± 0.72, 20.36 ± 3.28, 27.58 ± 4.09, and 41.62 5.83 after 48 h application in Control, CK, DDP, and CK + DDP groups, respectively. The result showed that the apoptosis may be due to reduction in level of p-Aky in PI3K/Akt pathway in all treatment groups. The results exhibited that proliferation stopped in MCF-7 cell line by CK and DDP through downregulation of the epithelial mesenchymal transition (EMT) process by increasing in the level of epithelial marker molecule E-cadherin, and reduce the level of mesenchymal markers N-cadherin and vimentin [49].

The ginseng role in cancer prevention is also verified in vivo study Ginsenoside Rg3 helps to increase the bioavailability of paclitaxel in animal-group and improved the anti-cancer activity in rats. The oral administration of paclitaxel with 20(s)-ginsenoside Rg3 could offer an effective strategy [50].

3.2. Ginseng and colon cancer

Colon cancer is a tumor growth in the rectum, appendix and colon. It is more common in men (72.5%) as compared to women (56%) [51]. According to 2012–2014 cancer data, 4.3% of people are at the risk of colon cancer. In 2017, 8% new cases of colon cancer and 8.4% death cases is reported [40]. By early detection we can reduce the mortality rate which is 65,000 deaths/ year [52]. Ginseng helps to treat the colon cancer. It was proven by case control study, which was conducted in Korean center hospital. This study included 111 cases of colon and rectum cancer and 118 were controls. The odd ration of ginseng effect on cancer was 0.42 [14].

Ginseng pharmaceutical components act in intestine and cause death of colon carcinoma cell in the body. The anti-cancer action of ginseng in case of colon cancer also proven by following pre-clinical trials. Ginseng has protopanoxidal (PPD) ginsenoside; once converted into 20-O-β-d-glucopyranosyl 20 (S) -protopanaxadiol (20-GPPD) by human intestinal flora could behave as anti-cancer agent [53], Which halts the growth of colon tumor cell in mice by causing the death of colon cancer cells via induction of cytoplasmic Ca2+ from Transient Receptor Potential Cation (TRPC) channels [54]. In vivo study, the colon cancer was induced in immuno-deficient nu/nu mice by giving azoxymethane [55] followed by dextran sulfate sodium (DSS). The mice were distributed into two groups, control group received western diet (20% fat) and treatment group received 0.85 mg /day of the 250 ppm ethanol-butanol extract of American ginseng with western diet for 12 weeks. There were significantly ($p < 0.05$) reduction in tumor multiplicity in treatment group (5.1 ± 23) as compared to control group (15.6 ± 2.3). American ginseng extract reduced the 50% proliferation and increased the 50% apoptosis in treatment group as compared to control group. American ginseng extract significantly reduced the up-regulations of Phospho-Active-EGFR (pEGFR), pErbB2, pERK, and pAKT in colon tumor as compare to the western diet control group. [56].

In another vitro study, ginsenoside GRh2 (100 μM) from American origin ginseng was applied on colecteral cancer cell line (HCT116) which in result significantly decreased ($p < 0.05$) the EGF- induced neoplastic transformation and inhibit the growth of HCT116 cells. GRh2 inhibited the activity of PBK/TOPK by directly bind to the PBK/TOPK. The inhibition of activity of PBK/TOPK suppressed the phosphorylation of ERK1/2 (81%) at 50 μM concentration of GRh2. However, in vivo study, when GRh2 were given (10 mg/kg or 50 mg/kg) three times a week for 26 days to HCT116 xenografted nude mice, it in result inhibited the growth of tumor cell to 49 and 78% relative to the control group. It also suppressed expression of the extracellular regulated protein histone H3 and kinases 1/2 phosphorylation level [57]. In human Colorectal carcinoma (CRC), ginsenoside 20(S)- and 20(R)-Rh2 also halted the proliferation of cancerous cell via inhibition of interleukin-6 signal and activation of STAT3 phosphorylation. That pharmacological activities of ginsenoside 20(S) was much higher than 20(R)-Rh2. It also increases the cytotoxicity activity of doxorubicin. The result proved that novel component of GRh2 can be used as therapeutic agent against metastatic colon cancer in combination treatment with other therapeutic agent [58]. In another study, Korean red ginseng extract (KRGE) under hypoxia condition showed 35–46% decrease in VEGF mRNA levels compared to the hypoxia control condition in HCT116 cells. KRGE controlled the epithelial to mesenchymal transition (EMT) of colorectal cancer cells (HT29 and HCT116) in hypoxic condition evaluated by western bolt and PCR analysis. KRGE also stopped the proliferation of colon cancer cell via down regulating the NF-kappa B and extracellular signal-regulated kinase1/2 pathways [59].Water extracted American ginseng (0–2 mg/mL) ginsenoside application on HCT116 p21-/- cell (colon cancer) for 6 days, reduced the cancer cell proliferation. The IC_{50} value for p21-/- was 0.46 ± 0.05 mg/mL as compared to it IC_{50} value for its wild type counterpart was 0.79 ± 0.044 mg/mL, which shown that p21-/- cells were more sensitive to inhibition effect of ginseng extract as compare too their wild type counterparts. At G_o/G_1 cell cycle phase, the ginsenoside of American ginseng arrested the cell growth via increasing the expression of tumor suppressor gene p53 and p21 and downregulate the levels of P-MEK [60]. Apoptosis action of ginseng on colon cancer is depicted in Fig. 3.

The other in vitro study told that, a metabolite of ginseng named as 20-O-β-d-glucopyranosyl-20(S)-protopanaxadiol (20-GPPD) induced apoptosis by regulation of cytoplasmic Ca^{2+}. However in vivo study 20-GPPD lowered the volume and number of colon cancer. Ginseng metabolite also decreased colon tumor through entry of Calcium chelator in tumor cell via transient receptor potential canonical (TRPC) and activation of AMP-activated protein kinase (AMPK) pathway [54]. In vivo study, when oral intake of American ginseng (30 mg/kg) for 90 days in mice with azoxymethane/dextran sodium sulfate-induced colon cancer, were Significantly reduced the total number of tumor ($p < 0.01$) and load of colon tumor ($p < 0.001$). American ginseng also downregulated the gene expression of inflammatory cytokines (interleukin-1α (IL-1α), IL-6, IL-1β), granulocyte-colony stimulating factor, tumor necrosis factor-α and granulocyte-macrophage colony-stimulating factor in colon and the small intestine. So, American ginseng potential is proven to be used as chemo preventive in colon cancer [61].

3.3. Ginseng and liver cancer

Liver cancer which start from liver is called hepatic cancer and which has spread from other part of body to the liver is called metastasis that is more common type of it. The main cause of liver cancer is cirrhosis due to alcohol, hepatitis B, hepatitis C and other cause include fatty liver, non-alcoholic fatty liver disease and aflatoxins. Liver cancer is more common in males as compared to females. The Hepatocellular tumor (70–85%) is more common in all type of liver cancers [62]. In 2017, 2.4% new cases of liver and intrahepatic bile duct cancer and 4.8% death cases is reported [40].

Ginseng help to treat the liver cancer as explained by following research studies. In a case control study, which included 264 cases and 269 control; the odd ration of effect of ginseng on liver cancer was 0.48 [14] Ginseng active ingredients includes ginsenoside, peptides, polysaccharides, oligosaccharides, polypeptides, fatty acids, amino acids, and aetherolea [63] from which oligosaccharide helps to promote the lymphocyte proliferation, increase phagocytosis, and enhance the production of tumor necrosis factor in macrophages. The anti-cancer mechanisms of ginseng in liver cancer is described with the help of different in vivo studies as given following. Water Soluble *Panax ginseng* Oligosaccharide (WGOS) was given to the ICR male mice carrying H22 ascites at different concentration levels (1,12.5,25 mg/kg) which in result reduced the tumor volume, 0.84,0.55 and 0.76 g respectively and inhibited the H22 induced tumor in ICR male mice with inhibitory ratios of 36.27%, 58.19% and 41.90%. WGOS (1, 12.5 and 25 mg/kg) can significantly elevated ($p < 0.01$) the serum tumor necrosis factor α (TNFα) levels as compared to model control group. WGOS also increased splenocyte proliferation, index of splenocyte proliferation reached at its peak at 12.5 mg concentration of WGOS in ICR male mice. The cytotoxic activity of natural killer cell (NK) helped in elimination of tumor cell. The cytotoxic activity of NK cell in WGOS (12.5 and 25 mg/kg) group was significantly increased ($p < 0.01$) as compared to model control group [64].

In a *vivo* study, when 2% ginseng [65] was introduced in the diet of rats with hepatocarcinogen induced by Diethyl nitrosamine significantly ($p < 0.05$) minimized the area of GST-P–positive foci (glutathione (S)-transferase P form–positive foci) about 62% and tumor number (68%) as compared to control group. The proliferation index of 2% GS group was significantly decreased to 4.67% ± 0.20% as compared to control group (5.44% ± 0.29%). GS group introduced apoptosis by altering the signaling pathway of p53 via downregulation of Igf-1, Cyclin G1, Cyclin D1 and Cdc2a expression [66]. Mechanism of action of ginseng against lung cancer is presented in Fig. 4.

The therapeutic effect of ginseng in liver cancer is proven from a study, in which ginseng (150 mg/Kg b.w) with Fumonisin in diet for 6–8 weeks and Aflatoxin B_1 were given orally for first 2 weeks to rats that in resultant improve the biochemical analysis by significantly increased in ALT, AST activity and urea with significant reduction in total protein and albumin and also improved the tumor markers, antioxidant capacity and histological examination of liver. [67].

3.4. Ginseng and lung cancer

Lung carcinoma is one of the most prevalent cancer in the world, around one-third of cancer is related to the lungs. Metastatic lung cancer patients survived only for 4–5 months and 10% patient life expectancy is one year [26]. According 2012–2014 cancer statistics report, 6.4% people are at the risk of lung cancer. In 2017, 13.2% of new cases and 25.9% mortalities of lung cancer is reported [40]

Ginseng has also been used for lung carcinoma patient because it helps to halt the proliferation and killing of the carcinoma cells in the body. A case-control study conduct in Korean National Hospital in which 276 cases and control are included. The odd ratio of ginseng against lung cancer was 0.55 [14]. The cohort study was conducted in ginseng cultivated area, Kangwah-eup in August 1987–December 1998 in which 4634 persons were included from 70.5% was ginseng user. The result of this study concluded that the relative risk of lung cancer among ginseng user is 0.30. There is no death reported among red ginseng user [12].

The findings of in vitro study indicated that silver nanoparticles with anti-microbial effect, can attached to cell membrane, increased the formation of reactive oxygen species and resulted in apoptosis [68]. *Panax ginseng* contains the silver nanoparticles which have anti-cancer effect on oncology patient. It helps to decrease the cell viability of lung (A549) by formation of Reactive Oxygen Species (ROS). These silver

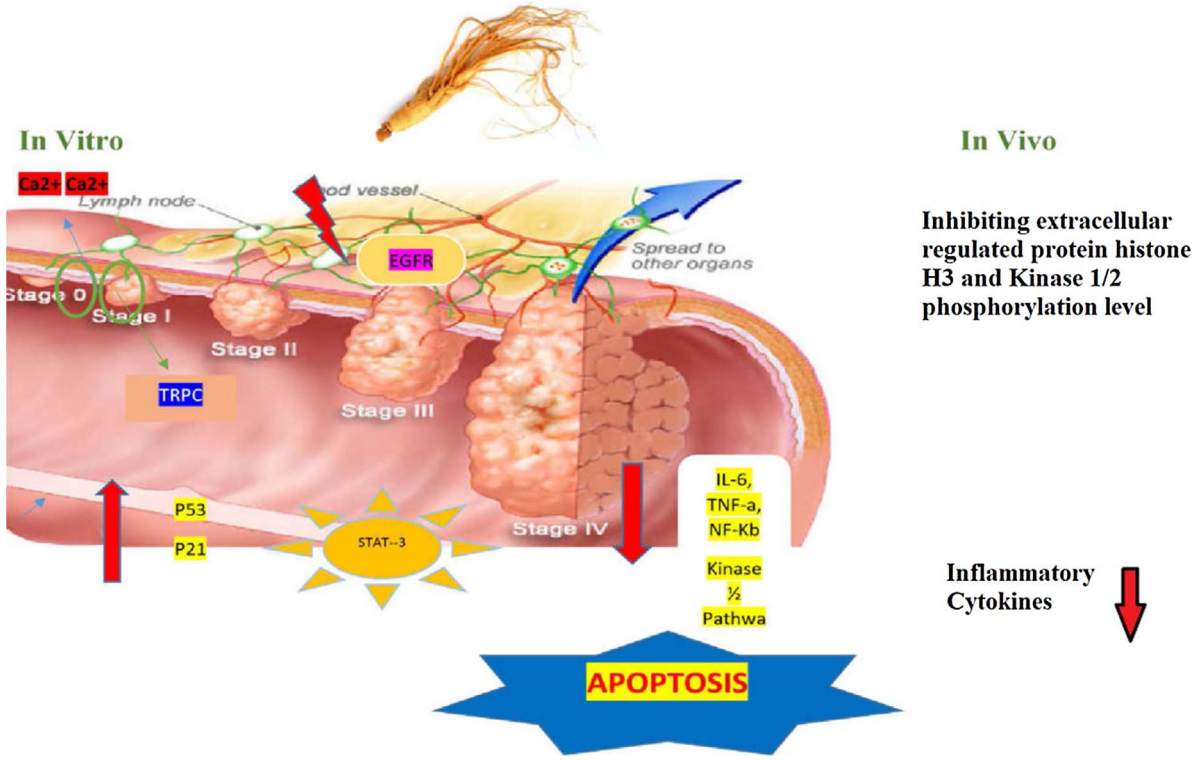

Fig. 3. In a vitro study, ginseng metabolites 20-GPPD decreased colon tumor through entry of Calcium chelator in tumor cell via transient receptor potential canonical (TRPC). Water extracted ginsenoside upregulate the tumor suppressor gene p53 and p21 at G0/G1 phase, Korean red ginseng extract down regulates the interleukine-6, TNF-α, NF-Kβ and kinase ½ pathway. Ginsenoside GRh2 activate the STAT-3. Ginseng compound K control the activation of proto-oncogene and proinflammatory gene via regulation of epidermal growth factor receptor. In Vivo study, Ginsenoside GRh2 induce apoptosis through inhibiting the extracellular regulated protein histone H3 and kinases 1/2 phosphorylation level and American ginseng downregulated the gene expression of inflammatory cytokines (interleukin-1α (IL-1α), IL-6, IL-1β), that all result in apoptosis of colon cancer cell.

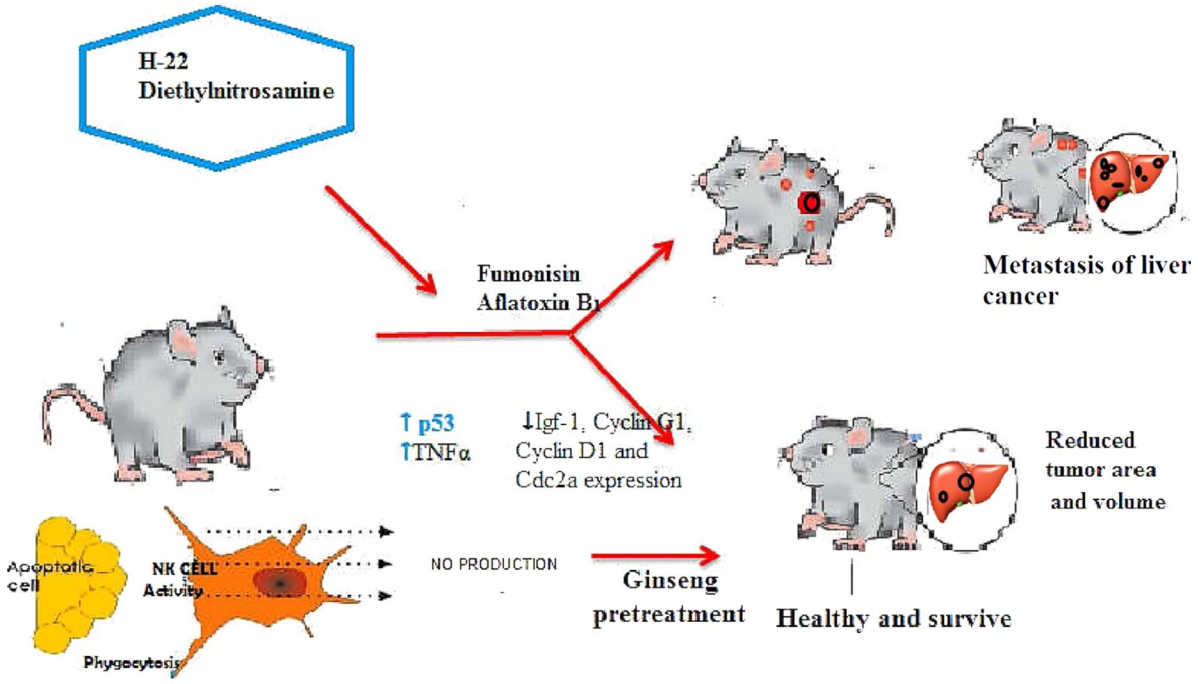

Fig. 4. The tumor number and area is reduced by giving 2% ginseng with diet to the rats through upregulation of gene p53 and TNF a level and down regulation of Igf-1, Cyclin G1, Cyclin D1 and Cdc2a expression. When ginseng given to the H-22 bearing mice the elevate the serum tumor necrosis factor α (TNFα) levels, lymphocyte proliferation in spleen, activity of natural killer cell, phagocytosis of apoptotic cell and produce NO secreted by scavenger cell in H22-bearing mice.

nanoparticles of ginseng also induced the cell death via halting the migration of Epidermal Growth Factor (EGF), lowering the phosphorylation of EGF receptor and decreasing the mRNA level. The nanoparticles of ginseng also stimulates the p38 MAPK/p53 pathway which increase the cell apoptosis and modify the morphology of cell nucleus [69]. Heat-steamed ginseng contains ginsenoside Rg5 and Rk1 which induced the apoptosis in the lung cancer cell (A549) via controlling Interleukin-2 (IL-2) and Glutathione (GSH) with increased production

Table 1
Ginseng anti-cancer action in different organ of body.

Ginseng Active Ingredient	Cells line/ Animal	Conc./Time	Result	Mechanism	Organ	Reference
Black fine hair ginseng, Rg5	MCF-7	25,50 μM for 48 h	• Activate the p38, MAPK pathway. • Dysregulation of Bax/Bcl2. • Activation of caspase-9. • Upregulate the p15INK4B, p53 and p21WAF1/CIP1 gene. • dysregulate of cyclin D1, CDk4 and cyclin E2.	Apoptosis, Anti-proliferative	Breast	Kim & Kim [42]
Panax ginseng, Rg5 (Shanghai Institute of Materia Medical of the Chinese Academy of Sciences (Shanghai, China).	BT-474, T47D	10 mg/mL for 48 h	• Promote the protein associated with AMPK pathway.	Anti-proliferative	Breast	Zou & Liu, [43]
Panax ginseng Rg3	Breast Cancer cell	30 μM for 24 h	• Block NF-kB factor signaling.	Antiproliferative and Apoptosis	Breast	Kim et al. [45]
Red American ginseng; Re, Rg2	MCF-7, MDAMB_23T	0.5 mg/mL for 2 h 0.2 mg/mL for 2 h	• Control the expression of cyclin A and cyclin D1.	Apoptosis and Antiproliferative	Breast	Wang et al. [44]
GF2 (obtained by conversion of Rb1 via intestinal bacteria)	Breast cancer stem cell	120 μM for 24 h	• Upregulate the p53 gene. • Activate the intrinsic apoptotic pathway and mitochondrial dysfunction.	Apoptosis	Breast	Mai et al. [47]
Compound K (obtained by incubation of protopanaxadiol type ginsenosides with Bacteroides JY-6, a human intestinal bacterium,	MCF-7 cells	35 μg/mL for 48 h	• ROS production. • Down regulation of Cox-2 expression and PGE level.	Antiproliferative, Apoptosis	Breast	Kim et al. [48]
Compound K (Weikeqi Biological Technology Co. (Shichuan, China) and cisplatin	MCF-7 cells	50 μmol/L for 24 h	• Inhibition of EMT. • Reduction in level of p-Aky in PI3K/Akt pathway.	Antiproliferative, Apoptosis	Breast	Zhang & Li [49]
Rg3 (Zhejiang Institute for Food and Drug Control)	BT-549, MDA-MB-231, MDA-MB-453	35 uM for 48,72 h	• Deactivate NF-kB. • Downregulate the expression of Bcl-2 and p65. • Upregulate Bax and caspase-3 expression.	Apoptosis	Breast	Yuan et al. [41]
20-GPPD (ginseng root methanol extraction, using a thermostable recombinant β-glycosidase from *Sulfolobus solfataricus*)	Colon cancer cell (CT-26)	20 μM for 24 h in murine cancer cell	• Induction of cytoplasmic Ca2 + from TRPC channel • Activate the AMPK pathway	Apoptosis	Colon	Hwang et al. [54]
American ginseng, Compound K	Male mice	0.85 mg/kg	• Regulate EGFR signal. • Down-regulation of Phospho-Active-EGFR (pEGFR), pErbB2, pERK, and pAKT.	Apoptosis and Antiproliferative	Colon	Dougherty et al. [56]
American ginseng, GRh2	HCT116, =	100 μM for 24 h	• Inhibit the activity of PBK/TOPK.	Apoptosis	Colon	Yang et al. [57]
American ginseng, GRh2	Nude mice	10,50 mg/kg	• Suppressed the expression of the protein histone H3 and kinases 1/2 phosphorylation level.	Antiproliferative	Colon	Yang et al. [57]
Panax ginseng, 20 (R) -Rh2	HCT116 and SW620	30 μM	• Inhibit IL-6 signal and activate STAT-3 phosphorylation.	Antiproliferative	Colon	Han et al. [58]
Korean red ginseng extract	HT29, HCT116	0.5–2 mg/mL for 24 h,72 h	• Control EMT of cancer cell in hypoxic condition. • Downregulate NF-kB, Kinase 1/2 pathways.	Antiproliferative	Colon	Kim et al. [59]
American ginseng root (Water extracted)	p21/- cell	0–2 mg/mL for 48 h	• Upregulate p53 and p21 gene and lower the PMEK level.	Apoptosis, Antiproliferative	Colon	King & Murphy [60]
20-GPPD (ginseng root methanol extraction, using a thermostable recombinant β-glycosidase from *Sulfolobus solfataricus*)	Mice xenografted with CT-26	0.2,0.5,1 mg/kg in mice	• Activate AMPK pathway and entry of Ca chelator in tumor cell.	Lower the number and volume of colon cancer cell	Colon	Hwang et al. [54]
American Ginseng	Male mice for 90 days	30 mg/kg	• Downregulation of inflammatory cytokines, TNF-a, granulocyte-macrophage colony stimulating factor.	Reduce the cancer initiation and Proliferation	Colon	Hwang et al. [54]

(*continued on next page*)

Table 1 (*continued*)

Ginseng Active Ingredient	Cells line/ Animal	Conc./Time	Result	Mechanism	Organ	Reference
Panax ginseng, WGOS	ICR male mice	12.5,25 mg/kg Body weight	• Increase TNF-a, lymphocyte proliferation in Spleen, activity of Natural killer cell, Phagocytosis and production of NO.	Restrict cancer cell growth	Liver	Yu et al. [61]
Korean red ginseng	Female Sprague–Dawley rats	150 mg/kg B.W	• Downregulate Igf-1, Cyclin G1, Cyclin D1 and Cdc2a expression.	Reduced the cancer area and Apoptosis	Liver	Jiao et al. [64]
Panax finseng fresh leaves (Silver Nano Particles)	A549 cells	5,10 μ/mL	• Induced the formation of ROS. • Halting the migration of EGF. • Lowering the Phosphorylation of EGF receptor. • Decreasing the mRNA level. • Stimulate the p38 MAPK/p53 pathway.	Apoptosis	Lung	Abdel-Wahhab et al. [67]
Sun ginseng, Rg5, Rk1	A549 cells	75,70 μM for 24 h	• Increased production of CMLs protein, Trans aldolase and PNPase. • Control the IL-2 and GOS.	Apoptosis	Lung	Castro-Aceituno et al. [69]
Korean red ginseng, Rg3- fortified red ginseng	H-460 cells	156–1250 g/ml	• Proliferation of splenocyte without affecting the production of NO.	Apoptosis	Lung	Kwak & Pyo [70]
100-300mg/kg Rg3-fortified red ginseng	Male ICR, BALB/c and nude mice	100 mg/kg for 7 day	• 30% decreased in tumor Volume and increased production of blood macrophage.	Apoptosis	Lung	Park et al. [78]
Rg3 (Dalian Fusheng Pharmaceutical Co., Ltd. (Dalian, China)	A549 cell, Nude mice	50,100 and 200 mg/ml at 12, 24 h 20 mg/kg	• Decreased cell viability. • Reduced the tumor volume and weight by halting p13k/Akt signaling pathway.	Apoptosis	Lung	Park et al. [78]
Panax ginseng, Compound K	Sk-MES-1, A549	IC_{50} = 16.53,17.78 μM for 24,48 h	• Increased protein level of IREIa, XBP-1S and GRP78/BiP. • Increase phosphorylation of elF2a.	Apoptosis	Lung	Kwak & Pyo [70]
Rg3, Rg5, Rk1(Ginseng Science Inc. (Seoul, Korea)	A549 cells, Normal human fetal lung fibroblast WI38 cells	< 100 μg/mL for 24 h	• Downregulation of Cyclin-D kinase-4, Cyclin-D kinase-6, Cyclin-D pRb. • Upregulation of p18 and p27. • Increased in tumor suppressor FOXO3a. • Activation of extrinsic Capase-9 FOXO3a/ caspase8/FasL and intrinsic caspase-9.	Apoptosis	Lung	Shin et al. [71]
Panax ginseng, 25-hydroxyprotopanaxadiol derivatives (x1, 1c and 8b)	H-460 cells, A549 cells	30,60 μM	• Downregulate the expression of B catenin signaling pathway.	Anti-proliferative	Lung	Yao et al. [72]
P. notoginseng, 20(S)-25-methoxyl-dammarane-3b,1B, 20 triol	A549, H358, H838	0–100 μM for 24 h	• Lowering the protein level associated with proliferation and halt the cell cycle at G1 phase.	Anti-proliferative, Apoptosis	Lung	Bi et al. [74]
Korean red ginseng root extract	Swiss albino mice	5, 10, 25, 50, 100, 200 mg/kg/ b.wt/day for 30 days	• Reduced the lipid peroxide level and increase the level of superoxide dismutase, vitamin C, total protein, catalase and reduced glutathione.	Reduced the no of tumor cell and reoccurrence of tumor	Skin	Bi et al. [74]
Panax ginseng, GOS	RAW 246.7 cells	250 μg/ml for 6 h.	• Increase in the production of TNF-a, NO and IL-6 and upregulate the C-jun N terminal kinase phosphorylation, p38, NK-kB and ERK signaling for cytokinesis.	Apoptosis	Skin	Sharma & Goyal [76]
Panax ginseng bioactive compound, GF2	Male C57BL/6 and IL-17A knock out (KO) mice	1 mg for 24 h	• Halt the production of ROS and IL-17 in neutrophils and γδ T cells.	Reduced the skin thickness and weight of sin punch	Skin	Seo et al. [77]

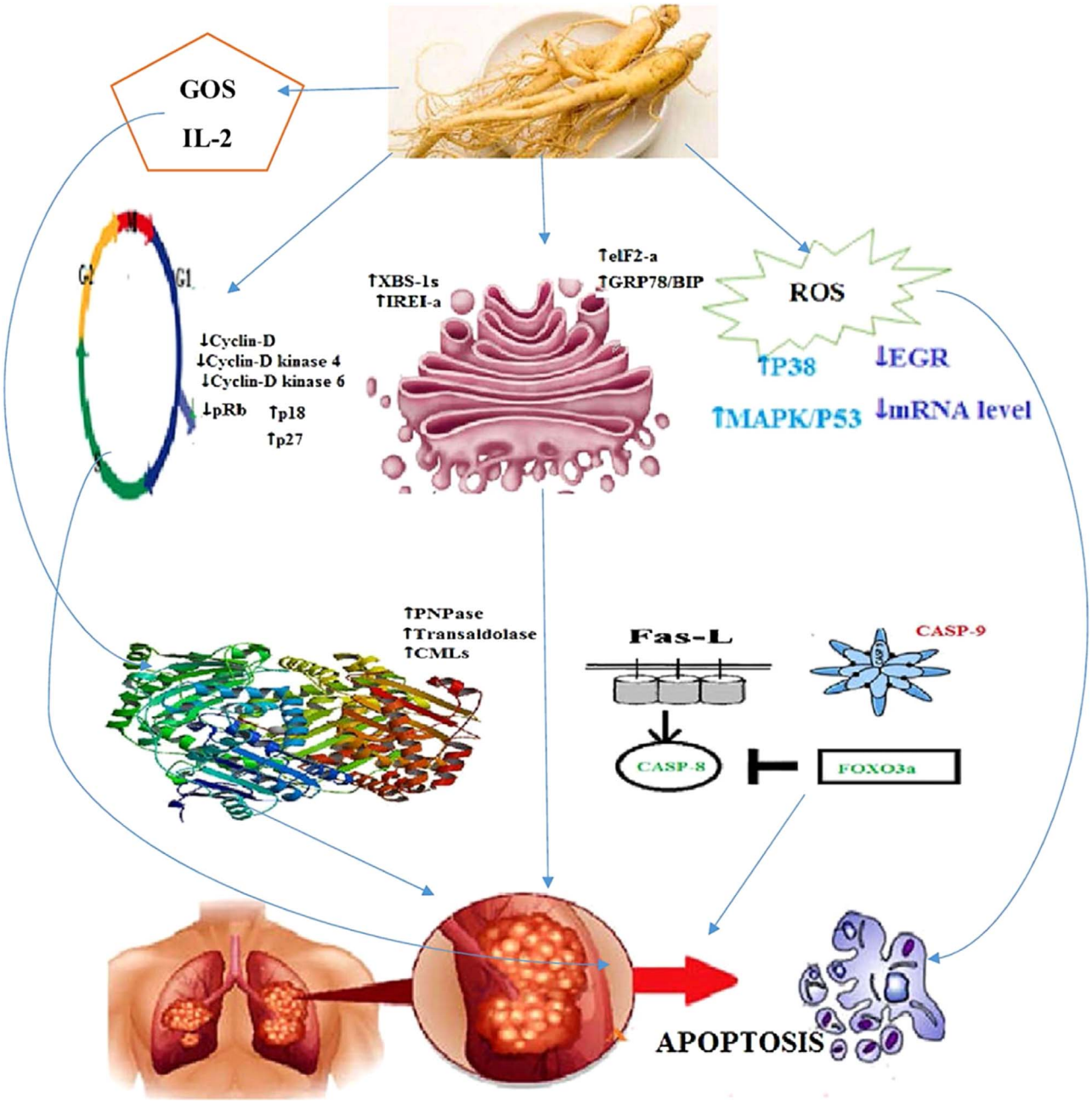

Fig. 5. Silver nanoparticle from ginseng produce reactive oxygen species which cause death in lung cancer cell via lowering the phosphorylation of EGF receptor and decreasing the mRNA level and upregulate the p38 and MAPK/p53 pathway. Ginseng compound K induced apoptosis in SK-ME(S)-1 and A549 human lung cancer cells by extended endoplasmic reticulum (ER) stress via increased protein levels of IRE1α, XBP-1S and GRP78/BiP and phosphorylation of eIF2α in lung cancer cells. In lung cancer cell, Ginsenoside Rg5 and Rk1 induces apoptosis via controlling interleukin-2 and glutathione with increased production of calmodulin-like protein, transaldolase and purine nucleoside phosphorylase. Ginsenoside Rg3, Rg5 and Rk1 induce apoptosis at G1 phase through downregulation of cyclin-D kinase-4, cyclin-D kinase-6, and phosphoretinoblastoma protein (pRb), upregulation of p18 and p27 and activate the extrinsic FOXO3a/caspase-8/FasL and intrinsic caspase-9.

of Calmodulin-like protein (CMLs), transaldolase (TAL) and Purine Nucleoside Phosphorylase (PNPase) [70].

In another in vitro study, Rg3- fortified red ginseng (Rg3-RGP) ($\geq$250 μg/mL) induced necrosis in Human non-small cell lung carcinoma cell line (H460) and enhanced the immunity modulation via increased proliferation of splenocytes (19–37%) without affecting the production of nitric oxide. Rg3-RGP also exerted a cytotoxicity in H-460 cells which is directly proportional to the concentration of Rg3-RGP. The IC_{50} value was 308 μg/mL for Rg3-RGP. [65]. In another study, ginsenoside Rg3 decreased the cell viability, impede the expression of p-PI3K/PI3K and p-Akt/Akt signaling pathway and introduced death in lung cancer cell lines A549 and H23 cells, which is investigated by CCK-8 kit, western blot and flow cytometry respectively. When Rg3 (50, 100 and 200 μg/mL) were added on A549 cell then it significantly reduced the cancer cell viability after treatment of 12 h and 24 h and in H23 cells, Rg3 (100,200 μg/mL) inhibit cell viability after 12 h treatment. However, in in vivo study, the H460 tumor-bearing mice decreased the tumor volume by 30–31% and increased the phagocytic index of peripheral blood macrophages via oral administration of 100–300 mg/kg of Rg3-fortified red ginseng preparation (Rg3-RGP) for 28 days [65]. In other vivo study, 3–4 week old nude mice were introduced lung cancer by A549 and H23 cells xenograft and divided into two group; control vector group received 0.1% DMSO and Ginseng group received Rg3 20 mg ginseng/kg body weight of mice. The ginseng group significantly

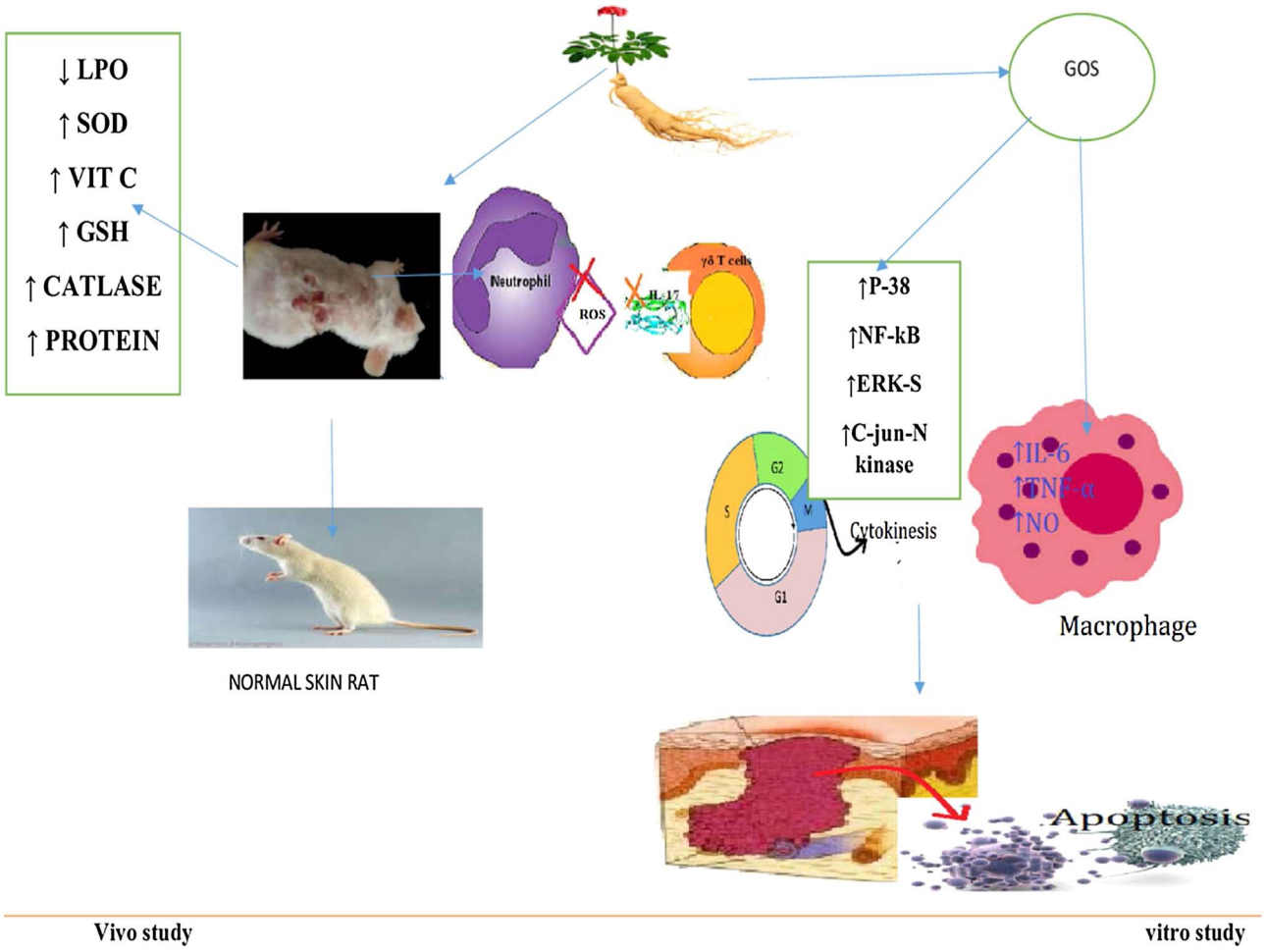

Fig. 6. When ginseng root extract applied on skin cancer it can reduced the number of tumor and prevent from reoccurrence. It also decreases the Lipid peroxide level and increase the level of superoxide dismutase (SOD), Vitamin C, total proteins, catalase and reduced glutathione in rats. The tumor volume also decreased by application of ginsenoside F2 via stopped production of Reactive oxygen species and Interleukin-17 and neutrophils and Gamma Delta T cells in rats. In a vitro study, apoptosis occurs by application of ginseng oligosaccharides on murine macrophage cells (RAW 26.7) which increase the production of tumor necrosis factor-alpha, nitric oxide and Interleukin 6 and up regulation of the C-Jun N-terminal kinase phosphorylation, p38, NF-kB and ERK signaling for cytokinesis.

($p < 0.05$) reduced the tumor volume and weight as compared to control vector group [55]. When 10 mg/kg dose of *Panax notoginseng* compound 20(S)-25-methoxyl-dammarane-3β, 12β, 20-triol (25-OCH3-PPD) were given for 6 weeks to the A549 xenografted nude mice, it results in inhibited tumor growth (> 35%) at $p < 0.01$. The 25-OCH3-PPD of ginseng can be used as novel therapeutic agent as it did not show any significant difference in body weight and not found any gross organ abnormality at necropsy. (Wang et al., 2009).

Pronouncement from other study depicted that ginseng compound K induced cytotoxicity in human lung adenoma carcinoma (A549) and Human lung squamous cell carcinoma (SK-ME(S)-1). The IC_{50} value was 17.78 μM and 16.53 μM, respectively. The cytotoxic effect of compound K on A549 and SK-ME(S)-1 was due to apoptosis which involved the caspase dependent pathway. The compound K also decreased the expression of anti-apoptotic proteins (c-FLIPL, X-linked IAP (XIAP), Bcl-2, and Bcl-xL). The result showing the associated activation of both extrinsic and intrinsic pathways of apoptosis. The molecular target of compound K apoptotic mechanisms was linked with extended endoplasmic reticulum (ER) stress via increased protein levels of IRE1α, XBP-1S and GRP78/BiP and phosphorylation of eIF2α and accumulation of the intracellular calcium in lung cancer cells [71]. At G_1 phase, ginseng enriched with Rg3, Rg5 and Rk1 administration halted the cell cycle and induced apoptosis via downregulation of cyclin-D kinase-4, cyclin-D kinase-6, and Phospho-Retinoblastoma protein (pRb); and upregulation of p18 and p27. These ginsenoside induced autophagy via increase in tumor suppressor FOXO3a in lung cancer cell A549. These ginsenosides also cause apoptosis of lung cancer cell via activation of the extrinsic FOXO3a/caspase-8/FasL and intrinsic caspase-9 [72]. Summary of mechanism of action of ginseng is different active components against variety of cancer is recapitulated in Table 1.

Ginsenoside Rg3 with low dose of cyclophosphamide in Lewis Lung Carcinoma (LLC) reduced the angiogenesis without overt toxicity. Rg3 is capable of specific blockade of activated EC cell survival mechanisms, which in result prevented the growth and metastasis of lung cancer (LLC). This study showed that the mean volume of tumor was significantly decreased (3426.03 ± 424.43 mm^3) as compared to the control group (12915.12 ± 1444.48 mm^3). The survival rate after tumor induction was also increased in treatment group in comparison with the control [73]. The compound from ginseng 25-hydroxyprotopanaxadiol derivatives (xl, 1c, and 8b) stopped the growth of H460 and A549 lung cancer cell via downregulation of the expression of β-catenin signaling pathway [74].

The 25-OHC3-PPD and Rg3 significantly decreased the cell viability of tumor cell in several human non-small cell lung cancer cell lines (A549, H358, and H838) and non-malignant (BEA(S)-2B) lung epithelial cells. The IC_{50} value (the concentration that impedes the survival of cells by 50%) of 25-OHC3-PPD was less than 20 μm for human non-small cancer cell line but IC_{50} value higher for BEA(S)-2B which was 24.62. 25-OHC3-PPD was decreased the A549 cell proliferation by more than 90% at 50 μM and in other cell line (H358, H838) the proliferation

of cell decreased by 70% at same concentration. But in case of BEA(S)-2B, 50% cell proliferation was inhibited at 25 μM concentration. The 25 μM concentration of 25-OHC3-PPD was also significantly ($p < 0.01$) increased the apoptosis in human non-small cell lung cancer cell lines. The 25-OCH3-PPD arrest the cell cycle at G1 phase and inhibit the cell cycle progression. The 25-OCH3-PPD downregulated the expression of E2F1, MDM2, Cyclin D1, Cyclin E, cdc25c and cdk4. Contrariwise, p21 expression was upregulated in A549 cells. Apoptosis action of ginseng on lung cancer is shown in Fig. 5.

3.5. Ginseng and skin cancer

Skin cancer spread rapidly in developed countries due to depletion of ozone layer and other environmental conditions [75]. In 2017, 5.2% of new cases of skin cancer and 1.6% death are reported. Approximately 2.2% of people are at the risk of skin cancer [40] *Panax ginseng* has the potentials to become a chemo preventive agent and helps in reduction of skin cancer cells. In an animal study, ginseng root extract of different doses (5 mg/kg body weight, 10 mg/kg, 50 mg/kg, 100 mg/kg, 200 mg/kg) given orally to find out its impact on skin cancer cells of mammals. It was found that GRE significantly lowered the number of tumor cells and reduced the tumor occurrence as compared to the carcinogen treated control group. Further, GRE treatment reduced the lipid peroxide levels in skin and increase the level of superoxide dismutase (SOD), Vitamin C, total proteins, catalase and reduced glutathione [76]. Apoptotic action of ginseng on skin cancer is presented in Fig. 6.

In vitro study, when GOS (Low molecular weight oligosaccharide) derived from degradation of ginseng polysaccharides by enzymatic mean, applied on RAW 246.7 cells, then as a resultant they increased the production of tumor necrosis factor-alpha, nitric oxide and Interleukin 6 in murine macrophage cells line. Western bolt analysis showed that the application of GOS up regulate the C-jun N-terminal kinase phosphorylation, p38, NF-kB and ERK signaling for cytokinesis. GOS from ginseng also induced cell death in B16F10 melanoma cell

In vitro study, GOS (Low molecular weight oligosaccharide) derived from degradation of ginseng polysaccharides by enzymatic mean, applied to RAW 246.7 cells, which induced the activation of signaling molecules, such as Akt, MAPKs, and NF-κB, in RAW 246.7 macrophage cells and increased the macrophage function by releasing TNF-*α* and stimulate the phosphorylation of Akt and MAPKs (ERK, JNK, and p38, and NF-κB). GOS shown indirect anticancer properties in B16F10 melanoma cell trough activation of macrophage function. The GO(S)-primed macrophages applied on B16F10 melanoma cells, then it reduced the cell viability as compared to GO(S)-untreated macrophage cells [77]. The ginsenoside F2 (GF2) applied on tetradecanoylphorbol-13-acetate (TPA) induced skin inflammation in mice for one day. The GF2 in result, reduced the skin thickness and weight of skin punch with stopping the production of Reactive oxygen species and Interleukin-17 and neutrophils and Gamma Delta T cells respectively, as compared to control TPA treated group. The result was comparable with the protective effects of dexamethasone on skin inflammation. So, GF2 has potential to be used as chemotherapeutic agent in inflammatory skin carcinoma [78].

4. Conclusion

Prevalence of cancer is increasing day by day and one of the burden in the society of developing countries. In recent years, CAM gain popularity to treat oncology patient. Ginseng can be more advantageous CAM product due to its synergic effect with chemotherapy. Ginseng can control many types of cancer e.g., liver, skin, breast, colon and lung by inducing apoptosis through different mechanisms, reducing the proliferation of cancerous cell and stopping the angiogenesis process which in result halt the metastasis of cancer. Ginseng can overcome the effect of cancer treatment by promoting hair growth, improving cognitive function, enhancing psychomotor performance, preventing normal cell damage and reducing fatigue proven through vitro and vivo studies. In clinical settings, it can be an open new avenue for the development of ideal drug with combination of other chemotherapeutic drugs in future.

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