Therapeutic and Clinical applications of Ginseng, Curcumin and Allicin

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Abstracts: The present review is based mainly on papers published between 2000 and 2020 and gives information about the properties of ginseng, curcumin and Allicin in chemical and biological systems and its possible role in preventing several diseases. The main aim of this review is to highlight its role as an immunopathological applications, also reported are bioactive properties that may influence the development of therapeutic products.

Therapeutic applications of Ginseng

Effect on Ovarian carcinoma
In this study, it was found that 10 mM–50 mM of ginsenoside-Rg5 affects the viability, migration and adhesion capacity of the ovarian cancer OCI-P9a culture cells. This effect occurred in a dose dependent manner. The mice with ovarian cancer were treated with 25 mg/kg of ginsenoside-Rg5 for one month. This resulted in reduction of tumor volume, as compared to control mice, the mice treated with ginsenoside-Rg5 showed no metastasis of the tumor. Ginsenoside-Rg5 significantly reduced the expression of fibroblast growth factor-8 (FGF8b) that were high in OCI-P9a cells. This indicates that the anti-cancer effect of ginsenoside Rg5 maybe related to FGF8b-associated pathways. In conclusion, ginsenoside Rg5 obtained from ginseng is a good candidate for the therapy of ovarian cancer.

Effect on Neurodegenerative disorders
Several studies have highlighted the potential to diminish the clinical outcomes of these disorders via the administration of herbal compounds, among which gintonin, a derivative of ginseng, has shown promising results. Gintonin is a noncarbohydrate/saponin that has been characterized as a lysophosphatidic acid receptor (LPA Receptor) ligand. Gintonin may cause a significant elevation in calcium levels [Ca2+]i intracellularly, which promotes calcium-mediated cellular effects via the modulation of ion channels and cell surface receptors, regulating the inflammatory effects. Years of research have suggested that gintonin has antioxidant and anti-inflammatory effects against different models of neurodegeneration, and these effects may be employed to tackle the neurological changes. Therefore, we collected the main scientific findings and comprehensively presented them, covering preparation, absorption, and receptor-mediated functions, including effects against Alzheimer’s disease models, Parkinson’s disease models, anxiety and depression-like models, and other neurological disorders, aiming to provide some insights for the possible usage of gintonin in the management of neurodegenerative conditions.

In conclusion, the ability of gintonin to modulate multiple aspects of neurodegenerative conditions, including antioxidant mechanisms, calcium regulation, anti-neuroinflammation, and the regulation of survival and apoptotic mechanisms, makes it suitable for the treatment of neurodegenerative conditions. Moreover, it has been suggested that it can potentiate LTP and regulate hippocampal neurogenesis. Its safety, efficacy, low cost and wide availability make it a candidate drug for the management of neurodegenerative disorders which merits further study, including in preclinical and clinical studies.

Effect on Symptoms of Alzheimer’s disease
Ginseng component contains lysophosphatidic acid and reduces the effect of Ad related brain neuropathies. Ginsenosides decrease amyloid b-protein (Ab) formation by inhibiting b- and g-secretase activity or by activating the nonamyloidogenic pathway, inhibit acetylcholinesterase activity and Ab induced neurotoxicity, and decrease Ab-induced production of reactive oxygen species and neuroinflammatory reactions. Oral administration of ginsenosides increases the expression levels of enzymes involved in acetylcholine synthesis in the brain and alleviates Ab-induced cholinergic deficits in AD models. Similarly, gintonin inhibits Ab-induced neurotoxicity and activates the nonamyloidogenic pathway to reduce Ab formation and to increase acetylcholine and choline acetyltransferase expression in the brain through lysophosphatidic acid receptors. Oral administration of gintonin attenuates brain amyloid plaque deposits, boosting hippocampal cholinergic systems and neurogenesis, thereby ameliorating learning and memory impairments. It also
improves cognitive functions in patients with AD. Ginsenosides and gintonin attenuate AD-related neuropathology through multiple routes.

This review focuses research demonstrating that ginseng constituents could be a candidate as an adjuvant for AD treatment. However, clinical investigations including efficacy and tolerability analyses may be necessary for the clinical acceptance of ginseng components in combination with conventional AD drugs.

**Immunomodulatory Effects**

Siberian ginseng (*Acanthopanax lenticonus*) is known to have immunomodulatory effects. The polysaccharides, glycoproteins and compounds in Siberian ginseng such as isograft, syringing, and eleuthero side E are shown to potentiate modulate immunological functions. But this is effective only when the extract is taken in an aqueous medium. The three main compounds that show immunomodulatory effect are:

**Isograft:** In the immunomodulatory aspect, isograft mainly exerts anti-inflammatory activity. Its profound effect in ameliorating enema and pain was mediated through the inhibition on LPS-induced production of the pro-inflammatory cytokines, including TNF-α and the phosphorylated mitogen activated protein kinase (MAPK) signalling molecules p38 and ERK1/2, from macrophages.

**Eleuthero side E:** Eleuthero side E is another lignan isolated from *Iwuji* (Siberian ginseng). It could attenuate aesthetic-induced cognitive dysfunction in aged animals and ameliorate diabetes by enhancing glucose uptake, improving insulin resistance and regulating glucose metabolism in type 2 diabetic mice. Using bioactivity-guided fractionation, it was also found to be the active constituent of *Iwuji* (Siberian ginseng) for combating fatigue.

**Syringing (Eleuthero side B):** Syringing, also named eleuthero side B, belongs to the lignan chemical compound group. Syringing is reported to possess anti-diabetic, anti-fatigue, sleep potentiating, neuroprotective as well as antioxidant activities.

**Role in inflammation**

Ginsenosides are natural steroid glycosides and triterpene saponins found exclusively in the plant genus Panax. Various ginsenosides have been identified, and their abilities to regulate inflammatory responses have been evaluated. These studies have suggested a link between ginsenosides and inflammasome activation in inflammatory responses. Some types of ginsenosides, including Rh1, Rg3, Rb1, compound K, choruses saponin I, Rg5, and Rg1, have been clearly demonstrated to inhibit inflammatory responses by suppressing the activation of various inflammasomes, including the NLRP3, NLRP1, and absent in melanoma 2 inflammasomes. Ginsenosides have also been shown to inhibit caspase-1 and to decrease the expression of IL-1β and IL-18. Given this body of evidence, the functional relationship between ginsenosides and inflammasome activation provides new insight into the understanding of the molecular mechanisms of ginsenoside mediated anti-inflammatory actions. This relationship also has applications regarding the development of anti-inflammatory remedies by ginsenoside-mediated targeting of inflammasomes, which could be used to prevent and treat inflammatory diseases.

**Cardiovascular diseases**

Panax ginseng, also called Asian or Korean ginseng, has long been traditionally used in Korea and China to treat various diseases. The major active ingredients of *Panax* ginseng are ginsenosides, which have been shown to have a variety of therapeutic effects, including antioxidation, anti-inflammatory, vasorelaxation, antiallergic, antidiabetic, and anticancer. To date, approximately 40 ginsenoside components have been reported. Current research is concentrating on using a single ginseng compound, one of the ginsenosides, instead of the total ginseng compounds, to determine the mechanisms of ginseng and ginsenosides. Recent in vitro and in vivo results show that ginseng has beneficial effects on cardiovascular and vascular diseases through efficacy, including antioxidation, control of vasomotor function, modulation of ion channels and signal transduction, improvement of lipid profiles, adjustment of blood pressure, improvement in cardiac function, and reduction in platelet adhesion.

**Clinical Trials on Ginseng**

**American Ginseng to Improve HIV-Associated Fatigue: A Randomized, Placebo-Controlled, Parallel Design, Multiple-Dose Clinical Trial**

Trial ID: NCT01500096

This study involved 96 patients over 18 years of age, with HIV-1 infection on stable antiretroviral therapy for at least 3 months. Two doses were given to the patients with placebo for each respective dose. This 4-week therapy consisted of 1000mg of ginseng compared with 1000 mg of placebo and another arm of 3000mg of ginseng compared with 3000mg of placebo. **The results showed decrease in fatigue which was analysed by the following questionnaires:** Fatigue Severity Score (FSS), Brief Fatigue Inventory (BFI), Epworth Sleepiness Scale (ESS), Patient Health Questionnaire 9 (PHQ9), Insomnia Severity Index (ISI), Medical Outcomes Study (MOS) HIV Health Survey, Clinical Global Impressions (CGI), and Patient-Reported Outcomes Measurement Information System (PROMIS) fatigue.

**American Ginseng Treatment for Multiple Sclerosis Related Fatigue**

Trial ID: NCT00754832

This clinical trial included 56 participants with MS as diagnosed by the McDonald criteria. The study consists of two arms that includes arm I with Period 1 with Ginseng therapy (100mg/day escalating to 400mg/day for 6 weeks) intervention; Washout Period with no drug; Period 2 with placebo and arm II Period 1 with placebo; Washout period with no drug; Period 2 with ginseng therapy (100mg/day escalating to 400mg/day for 6 weeks) intervention. **There was no significant difference in the fatigue score measured by the Realtime Digital Fatigue Score.**

**Anti-fatigue Effect of Korean Red Ginseng in Patients with Non-alcoholic Hepatitis**

Trial ID: NCT02331589

In this study, 75 participants between the ages of 18 to 80 years with non-alcoholic hepatitis. The study consists of two arms: arm I (Korean Red ginseng capsule with 3,000 mg/day for 3
weeks) and arm II (placebo). There is no effect of Korean red ginseng on the fatigue levels of non-alcoholic hepatitis patients as measured by the by KRUPP's Fatigue Severity Scale.

American Ginseng in Treating Patients With Fatigue Caused by Cancer

Trial ID: NCT00719563

This study included 364 participants that were divided in two arms i.e. arm I (Patients received oral American ginseng twice daily for 14 days. This treatment was repeated every two weeks for 4 courses, for a total of 8 weeks of treatment) and arm II (Patients received oral placebo twice daily for 14 days. This treatment was repeated every two weeks for 4 courses, for a total of 8 weeks of treatment). The patients that received American ginseng reported less fatigue than the patients that were given placebo measured on the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF) general subscale.

Randomized Clinical Trial of Bococizumab (PF-04950615; RN316) in Subjects with Primary Hyperlipidaemia or Mixed Dyslipidaemia at Risk of Cardiovascular Events (SPIRE-LL)

Trial ID: NCT02100514

In this study, 746 participants were included in the 52 Week Phase 3 Double-blind, Randomized, Placebo-controlled, Parallel-group Study to Assess the Efficacy, Safety And Tolerability Of PF-04950615 In Subjects With Primary Hyperlipidaemia Or Mixed Dyslipidaemia At Risk Of Cardiovascular Events. The two experimental arms of this included arm I (Bococizumab (PF-04950615; RN316) 150 mg every 2 weeks, subcutaneous injection for 52 weeks) and arm II (placebo). The results suggested that there was a significant difference in Fasting Low-Density Lipoprotein Cholesterol (LDL-C) at Week 12 in the patient’s hat were given Bococizumab than the patients who received placebo.

Effect of TU-100 in Patients Undergoing Laparoscopic Colectomy (TU100P2T3)

Trial ID: NCT02232893

TU-100 is produced from three botanical raw materials i.e. Asian Ginseng, Zanthoxylum fruit (Japanese pepper), and ginger. The aim of this study is to assess the effect of TU-100 on post-operative quality of life during the 4 week postoperative period after straight, hand-assisted, or robot-assisted laparoscopic colectomy. Optimal efficacy parameters for subsequent outcome studies also will be explored. The study included 69 participants that were divided in two arms, arm I (5g TID (15g/day) of TU-100) and arm II (placebo).

American Ginseng Extract in Preventing Respiratory Infection and in Reducing Antibiotic Use in Patients With CLL

Trial ID: NCT00752895

The primary objective of this study was to assess the effect of American ginseng extract on the number of days of acute respiratory infection (ARI) during the peak respiratory illness season (January-March) in patients with chronic lymphocytic leukaemia (CLL) along with determine the its safety. In this study, 293 participants were divided into two arms i.e. Arm I (oral American ginseng extract twice daily) and Arm II (placebo). The patients that were given the dose of American ginseng had more ARI (acute respiratory infection) days than the patients that were given the placebo. But the number of antibiotic use days were less in the case of patients taking the dose of American ginseng twice a day.

Korean Red Ginseng and Metabolic Syndrome

Trial ID: NCT00976274

The primary objective of this trial was to observer the change in pre and post treatment systolic blood pressure for the period of 12 weeks. This trial included 60 participants. The study had two arms i.e Arm I (placebo containing starch 5 capsules three times every day for 12 weeks) and Arm II (Korean red ginseng 5 capsules (300 mg/capsule) three times every day for 12 weeks).

There was no significant difference between the blood pressure of the patients that were given the American ginseng and the patients given the placebo.

Efficacy Study of Korean Red Ginseng to Treat Depression

Trial ID: NCT01496248

The main purpose of this study was to determine whether Korean Red Ginseng are effective in the treatment of the residual symptoms of depression as an adjuvant treatment. The study included 35 participants that were given Korean Red ginseng (2g/day). The progress of the patients was measured on the Depression Residual Symptom Scale which showed a significant reduction in the symptoms of depression from the baseline.

Effect of Korean Red Ginseng (KRG) on Dry Mouth

Trial ID: NCT00911768

The primary objective of the study was to observe the effect of Korean Red Ginseng powder on Dry mouth and salivary flow rates in the Xerostomia population. The study included 100 participants that were divide in two arms i.e. Arm I (Panax ginseng : 6 g per day (twice a day)) and Arm II (placebo).

The results indicate that the Korean Red Ginseng in fact increased xerostomia that was measured on the Visual Analogue Scale of Subjective Dry Mouth.

Therapeutic application of curcumin

Anticancer activity of curcumin

Curcumin, a phenolic compound from the plant Curcuma longa L., has shown a wide spectrum of Chemo preventive, antioxidant and antitumor properties. Curcumin, a common flavouring agent in the spice turmeric, perturbs microtubule assembly dynamics through tubulin binding, it suppresses cell proliferation in a variety of cancer cell lines, and it inhibits
tumor genesis. Although Curcumin has an evident anti-cancer activity, relative poor stability has been highlighted as one of the major problems in Therapeutic applications. To enhance metabolic stability and ant proliferative activity against human cancer cells, various Curcumin analogy have been synthesized, among which bisdemethoxycurcumin (bodice) and diacetyl Curcumin (DAC). DAC shows higher cytotoxicity against human ovarian cancer cell Line, increased ant mutagenic, ant carcinogenic and antioxidant activity. The synthetic derivative DAC shows higher antibacterial activity against multi resistant bacteria and a stronger nitric oxide (NO) and O2 anion scavenging activity

The therapeutic effect of curcumin results from its chemical structure and unique physicochemical properties. Curcumin (IUPAC: 1E, 6E) – 1, 7-Bis (4-hydroxy-3-methoxyphenyl) hepta-1, 6-diene-3, 5-dione) contains two ferulic acid residues joined by a methylene bridge. The most important structural features related to the curcumin biological activity are: the o-methoxyphenol and methylene group responsible for the curcumin antioxidant activity. The formation of hydrogen bonds and the hydrophobicity of curcumin resulting from the presence of aromatic and tautomeric structures together with the flexibility of linking groups are responsible for its non-covalent interactions. Covalent interactions with protein thioles are enabled by α-unsaturated bonds and β-dike tone. In addition, the β-diketone- group forms complexes with transition metals, reducing the toxicity of these metals and their pro-oxidative activity

### Gastric cancer

Arsenic chronic exposure is known as a potential risk factor for developing oncological diseases such as gastric cancer. Results of some clinical trials suggested that curcumin can suppress carcinogen effects. For example, Biswas et al. found that curcumin application may reduce chronic arsenic exposure.

Tu et al. found that curcumin application led to decreased association of myeloid-derived suppressor cells (supressor of T-cell activation) in tumor tissue. It was observed that mobilization and activation of MDSCs are critical early events for IL-18-induced gastric carcinogenesis. This agent also interferes with MDSC-mediated stimulation of gastric cancer cells through inhibition of IL-6 secretion. In this line curcumin application to patients with gastric cancer leads to significantly decrease blood level of IL-6.

It is well known that distant metastasis via lymphatic invasion of cancer cells is a major reason for the poor survival of gastric cancer patients. Nevertheless, Da et al. found that curcumin application suppressed the expression of metastatic factors, such as LYVE-1 and VEGFR-3, both playing important part in the gastric carcinogenesis. LYVE-1 expression correlates with per neural invasion and lymphatic invasion. VEGFR-3 expression in the gastric mucosa is associated with poor survival, and its inhibition suppresses lymph node metastasis in vitro and in vivo in gastric cancer models. The effect of curcumin on tumor growth and development, specifically angiogenesis and invasiveness, is not negligible. Its application can lead to the suppression of VEGF pathways and the expression of matrix metalloproteinase (MMPs). VEGF signalling pathways are known as strong supporters and inducers of angiogenesis. MMPs support spreading cancer cells in gastric tissue by degradation of the extracellular matrix.

Another important curcumin effect on the environment of gastric tumours can be the regulation of gastric ph. It is known that an acidic ph can support cancer development. In gastric cancer, this phenomenon is associated with the expression of gastrin, a protein inducer of acid secretion. In vivo Zhou et al. found that curcumin application lowers gastrin secretion to elevate gastric fluid pH and thereby suppress gastric cancer cell proliferation.

### Influence of curcumin co-application on chemotherapeutic efficacy

5-fluorouracil, especially in combination with oxaliplatin significant problems of this method include inconvenience, toxicity, and cost addition of nontoxic agents, such as curcumin, enhances treatment effects. High potential of this approach was shown by Zhou et al. They proved that curcumin also led to stimulation of caspasas (3, 8, and 9), Bax and Bcl-2 suppression, apoptosis induction and inhibition of tumor growth. Co-application of extracts from Curcumin longa on the docetaxel-cisplatin-5-fluorouracil chemotherapy was studied by et al Panahi. Authors showed, that this approach significantly improved quality of life assessment. His approach significantly improved quality of life assessment (more than five times than placebo). This effect was coupled with a reduction of proinflammatory factors such as IL-6, TNF-α TGF-β and hs-CRP (negative marker of patient survival) in blood. Tang et al. found that curcumin application can suppress the function and expression of P-glycoproteins

### Application of drug delivery systems for curcumin targeting of gastric cancer

DDS for the transport of curcumin and epoxide could be based on lipid nanoparticles (glycerol monostearate, soybean phosphatidylcholine and oleic acid), as was designed by Jiang et al. Other studied strategies for curcumin targeting gastric cancer are represented by the application of metal and semiconductor nanoparticles, such as ZnO nanoparticles. The potential utility of this strategy was evaluated by Dhivia et al. ZnO nanoparticles display low water solubility, but it can be significantly improved by their surface modification with PMMA-PEG and Tween 80. Also Curcumin cyclodextrin complexes have significantly improved water stability, especially under alkaline condition.

### Pancreatic cancer

Curcumin causes G2/M cell cycle arrest in pancreatic cancer cells following DNA damage and ATM-Chk1-dependent inhibition of CDK-1 and Cyclin B1 activity. Curcumin also has potent effects on cell survival, most notably through regulation of the inhibitor of apoptosis (IAP) family, which includes Survivin, cellular IAPs 1 and 2 (cIAP1 and cIAP2) and X-chromosome linked IAP (XIAP). Curcumin abolishes Survivin, cIAP1 and 2, and XIAP protein and mRNA expression in pancreatic cancer cells. Inhibition of the ATP-dependent multidrug resistance protein-5 (MRP5), an efflux pump notorious for promoting the export of chemotherapeutic drugs. Interestingly, curcumin has been shown to suppress the activity of MRP5 and enhance the effects of 5-fluorourasil (5-FU) in pancreatic cancer.

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Immunomodulatory Effects of Curcumin

Many evidence suggest that the disorder of inflammatory pathways play a key role in cancer development, Curcumin suppress NF-κB activity by inhibiting the phosphorylation by I kappa B kinase (IkB) and impeding nuclear translocation of the NF-κB p65 subunit. Similarly, the transcriptional factor AP-1 (Activator Protein-1), known to be related to anti-apoptotic, mitogenic, and pro-angiogenic genes, is down regulated by curcumin. One member of the STAT family, STAT3, is described as a common target for several signalling pathways regulating oncogenes, STAT3 is reported to be a molecular target of curcumin in several tumours, both directly and indirectly by inhibition of IL-6. Tumor necrosis factor alpha activates NF-κB, then inflammatory genes (5-LOX, COX-2), inflammatory cytokines, molecules that adhere to cells, and inducible nitric oxide synthase (iNOS) are expressed. Therefore, the transcription of TNF-α and, thus, the expression of inflammatory genes are blocked by curcumin.

Breast Cancer

In the proliferation of breast cancer cells, NF-κB—the proinflammatory transcription factor—plays a key role. Curcumin displayed the ability to affect the breast cancer cell proliferation and invasion by down regulating the NF-κB inducing genes. Another target that acts on the proliferation of breast cancer cells is the human epidermal growth factor receptor 2 (HER2), a tyrosine kinase (TK) receptor belonging to EGFR family. The HER2 is considered as a drug target for cancer therapy since its overexpression is involved in the development of many types of cancer. Curcumin, alone or in combination with its analogues, may inhibit breast cancer cell lines though inhibiting of HER2-TK. The alterations (mutation and amplification) in the protein kinase B, named Akt, are related to carcinogenesis. Together with Akt, mTor (kinase) interfered in the control of cancer cell growth and proliferation. In breast cancer cells, curcumin down regulated Akt protein in a dose- and time-dependent manner, and induced autophagy and suppression of the ubiquitin-proteasome pathway. Ant proliferative abilities of curcumin are oestrogen dependent in ER (oestrogen receptor)-positive MCF-7 breast cancer cells. Indeed, it represses the expression of ER in downstream genes such as p52 and TGF-beta (transforming growth factor) in ER-positive MCF-7 cells, and this capacity is also dependent on the presence of oestrogen.

Lung Cancer

Curcumin exhibited its therapeutic efficiency in lung cancer treatment by means of the down regulation of NF-κB in human lung cancer cell lines A549 and by acting on the JAK2/STAT3 signalling pathway, inhibiting JAK2 activity. Moreover, curcumin inhibited cell proliferation and induced apoptosis of human non-small cell lung cancer cells via the up regulation of microRNA-192-5p and suppression of the PI3K/Akt signalling pathway. In lung tumor proliferation, neutrophil elastase (an important regulator of inflammatory processes) and α1-antitrypsin (natural inhibitor of neutrophil elastase) play prominent roles in the inflammation mechanism and curcumin repressed neutrophil elastase-induced tumor proliferation via up regulating α1-antitrypsin expression in vitro and in vivo. Curcumin also exhibited its proapoptotic activity in lung adenocarcinoma cells by suppressing expression of COX-2, EGFR, and extracellular signal-regulated kinase (ERK) 1/2 activities, which correlated with elevated apoptosis and reduced survival of lung adenocarcinoma cells.

Haematological Cancers

Curcumin has been found to suppress TNF-α-induced nuclear translocation and DNA binding of NF-κB through suppression of IκBα phosphorylation and degradation in the human myeloid ML-1a cells. The Wilms tumor 1 (WT1) gene acts both as an oncogene and as a tumor suppressor. It is involved in the proliferation and vitality of different cancer cells. It was found to be highly expressed in many leukemic cell lines and in patients with acute myeloid leukaemia. Curcumin inhibited cell proliferation and clonogenicity in the K562 cell line which expresses WT1 at a high level (mRNA and protein)—depending on time and dose—through inhibition of the WT1 protein. Curcumin also induced apoptosis through the activation of the JNK/ERK/AP1 pathways in human acute monocytic leukaemia THP-1 cells.

Multiple myeloma (MM) is a systemic malignant disease of the blood—in most cases fatal. Curcumin exerted its anticancer potential in multiple myeloma by acting on NF-κB and STAT3 cell signalling pathways. Indeed, curcumin exhibited anticancer potency by means of suppression of IκB kinase and its oral administration was reported to suppress NF-κB in PBMCs (peripheral blood mononuclear cells) from multiple-myeloma patients (5).

Anti-Alzheimer’s activity of curcumin

One current strategy for treating AD is anti-amyloid treatments including decreasing Aβ production, inhibiting Aβ aggregation, and promoting Aβ clearance. In vitro studies have shown that curcumin lowers Aβ levels by attenuating amyloid precursor protein maturation and suppressing beta-secretase 1 (BACE1) expression, which is the sole B-secretase enzyme. Recent studies have investigated the molecular mechanism of BACE-1 inhibition by curcumin. Apart from its role in amyloid precursor protein maturation, studies have indicated that curcumin can attach to Aβ peptides and prevent Aβ aggregation in vitro and in vivo. Alternative theories suggest that curcumin blocks Aβ aggregation by chelating metal ions, such as Cu2+, Zn2+, and Fe3+, likely agonists of Aβ aggregation and oxidative stress.

Effect of curcumin on neuroinflammation

Curcumin targets numerous inflammatory signalling pathways, including biosynthesis and metabolism of arachidonic acid, pattern recognition receptor pathways on the surface of glial cells, and nuclear transcription factors. Recent studies have suggested that curcumin attenuates neurotoxicity and the related inflammatory response by suppressing nucleotide-binding oligomerization domain (NOD)-like receptor protein 3 (NLRP3) inflammasome activation (Gong et al., 2015; Li et al., 2015). Curcumin may also act as an agonist of both peroxisome proliferator-activated receptor γ and nuclear factor erythroid-2 related factor 2, which regulate expression of various inflammatory cytokines. Curcumin has excellent antioxidant properties, which elevate superoxide dismutase and catalase activity to conserve glutathione levels and decrease malonyl dialdehyde accumulation in mouse models. However, elevated homocysteine plasma levels also led to abnormal DNA methylation, resulting in decline of cognitive performance (Fox...
Curcumin inhibits DNA methyltransferase and may be responsible for its ability to improve cognitive impairment.

**Antioxidant Properties of Curcumin**

In vitro, curcumin can significantly inhibit the generation of reactive oxygen species (ROS) such as superoxide anions, hydrogen peroxide and nitrite radical generated by activated macrophages, which play an important role in inflammation. It exerts powerful inhibitory effect against hydrogen peroxide-induced damage in human keratinocytes and fibroblasts. It has been reported that curcumin prevents oxidative damage during indomethacin-induced gastric lesion not only by scavenging of hydrogen peroxide and OH group but also by blocking inactivation of gastric peroxidase. Because ROS have been implicated in the development of various pathological conditions.

**Anti-inflammatory activity of curcumin**

the mechanism of action, curcumin has been found to inhibit cyclooxygenase 2 (COX-2) as well as lipoxygenase (LOX), two enzymes involved in inflammation (S1). Cytokine-induced COX-2 transforms arachidonic acid into prostaglandins during acute inflammatory episode. COX-2 is also the prevalent isoform during chronic inflammation. Lipoxygenase transforms arachidonic acid into leukotrienes, which take part in leukocyte recruitment and play a role in inflammation. The action of lipoxygenase is also attributed to colon carcinogenesis, which is described below in the section on the anticancer activity of curcumin.

**Clinical trials on curcumin**

**Oral Curcumin for Radiation Dermatitis**

Trial id - NCT01246973

The study involved 686 participants from age 21 Years to 120 Years (only females) with Radiation-induced Dermatitis criteria. The entire participants were under two arms (arm I – 4 Curcumin C3 Complex 500mg capsules (2.0 g) taken orally 3 times/day throughout course of radiation treatments plus one weekend arm II placebo). Moist desquamation was measured by the presence of wet, patchy crusting, oozing, or ulcerated skin in areas where skin was peeling in sheets. With objective to examine the efficacy of curcumin in preventing and/or reducing the severity of dermatitis in radiation treatment site in breast cancer patients. The RDS score ranges from 0-4 with higher scores indicating worse outcome.

**Curcumin as a Novel Treatment to Improve Cognitive Dysfunction in Schizophrenia**

Trial id - NCT02104752

The study involved 39 participants from age 18 Years to 65 Years with DSM-5 diagnosis of schizophrenia. The entire participants were under two arms Experimental: Curcumin, Curcumin capsules (Teralumen formulation of curcumin nanoparticles). Subjects randomized to curcumin will receive 360 mg/day (divided into twice daily oral doses). Intervention: Drug: Curcumin, Placebo Comparator: Sugar Pill Matched placebo, 2 capsules twice daily. Intervention: Drug: Placebo. This battery was developed as part of the National Institute of Mental Health (NIMH) sponsored Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Initiative to assess cognition in clinical trials of cognition enhancing drugs. The MCCB comprises 10 tests that assess 7 cognitive domains (speed of processing, verbal memory, visual memory, working memory, reasoning and problem solving, attention/vigilance, and social cognition). The MCCB takes approximately 65 minutes to administer and provides age and gender-corrected normed T-scores, including a global composite score and cognitive domain scores. The range of T-scores is between 0 to 100 with a mean of 50. Higher scores indicate better overall cognitive functioning.

**Curcumin (Diferuloylmethane Derivative) With or Without piperine in Patients with Multiple Myeloma**

NCT00113841

The study involved 42 participants with Multiple Myeloma. The entire participants were under two arms Curcumin starting dose 2 grams orally in 2 divided doses (a.m., p.m.). And Curcumin starting dose 2 grams orally in 2 divided doses (a.m., p.m.) and Bioperine 5 mg orally twice daily. The primary outcome was percent Change of NF-kB Protein Expression in Peripheral Blood-Mononuclear Cells from Baseline through 4 Weeks of Treatment [Time Frame: Baseline through 4 weeks of treatment. Curcumin + Bioperine shows Percent reduction more as compared to curcumin alone so it was concluded that group 2 is better.

**Dietary Supplement of Curcumin in Subjects with Active Relapsing Multiple Sclerosis Treated with Subcutaneous Interferon Beta 1a (CONTAIN)**

ID – NCT01514370

The study involved 80 participants with age 18 Years to 60 Years having Multiple Sclerosis. The entire participants were under two arms, 40 subjects with Interferon (IFN) beta 1 a 44 mcg TIW + Curcumin (BCM 95) and 40 subjects with IFN beta-1a 44 mcg TIW + placebo. Primary outcome was A single T2 lesion was defined as an area of increased signal on a given 3-millimeters axial image that was not referable to normally hyper intense structures. New T2 lesions were those that appear in areas where on the previous scan no abnormality was detected. All T2 lesions were detected by an MRI scan.

**18-Month Study of Memory Effects of Curcumin (Curcumin)**

ID – NCT01383161

The study involved 46 participants with age 50 Years to 90 Years having age-related cognitive impairment. The entire participants were under two arms, placebo i.e. sugar pill (Six capsules per day for 18 months.) or the curcumin supplement (Theracurmin®, containing 90 mg of curcumin). Six Theracurmin capsules (containing 30 mg of curcumin each) per day for 18 months. People with age-related cognitive decline (e.g., MCI, AAMI or normal aging) who receive a daily dietary supplement (curcumin) along with healthy lifestyle counseling (proper nutrition, exercise, etc.), will show less build-up of abnormal amyloid protein deposits (as measured with FDDNP-PET imaging) than those receiving placebo after eighteen months. Current Primary Outcome, Change from Baseline to 18 Months
on Brief Visual Memory Test-Revised, Recall and range from 0 to 36, with higher scores indicating better learning

- Change from Baseline to 18 Months on Brief Visual Memory Test-Revised, Delay Scores range from 0 to 12 and reflect recent, long-term learning, with higher scores indicating better learning.

- Change from Baseline on Buschke Selective Reminding Task, Consistent Long-Term Retrieval Scores indicate the sum of consistent long-term word retrieval across the 12 trials and range from 0 to 144.

- Change from Baseline on Buschke Selective Reminding Task, Total Score Scores range from 0 to 144.

- Secondary Outcome Trail Making Test is a measure used to assess cognition and attention. Beck Depression Inventory total scores range from 0 (no depressive symptoms) to 84 (extreme depression).

**Study to See How Safe Curcumin is and How Well it Works When Used to Treat Mucositis in Patients Getting Chemotherapy** NCT02300727

The study involved 6 participants 18 Years and older having ≥ grade 2 oral Mucositis related to chemotherapy for cancer.

The entire participants were under 2 arms first is Mouthwash-standard pharmacy preparation, second is Curcumin (BCM-95) administered by ingested mouth rinse three times per day. Curcumin-MTD There will be 3 participant at each of 4 does levels (0.33g, 1g, 2g, 3g) per rinse, three times daily for 4-6 weeks. (Additional 3 subjects if a dose-limiting toxicity occurs)

**Intervention: Drug:** Curcumin-MTD. Result - Insufficient data to analyse

**Curcumin for the Prevention of Radiation-induced Dermatitis in Breast Cancer Patients**

The study involved 35 participants with 21 Years and older females. The entire participants were under two arms Active Comparator: Curcumin C3 Complex Patients take 2.0 grams curcumin (four 500mg capsules) three times daily by mouth for prescribed course of radiation treatment (~4-7 weeks). Intervention: Drug: Curcumin C3 Complex Placebo Comparator: Placebo Patients take 2.0 grams placebo (four 500mg capsules) three times daily by mouth for prescribed course of radiation treatment (~4-7 weeks).

**Intervention: Drug:** Placebo.

The severity of radiation dermatitis was measured using the Radiation Dermatitis Severity (RDS) Scale which ranges from 0.0 to 4.0 with increments of 0.5. Results shows that patients with curcumin shows less dermatitis compared to placebo.

**Curcumin in Treating Patients with Familial Adenomatous Polyposis**

The study involved 44 Patients 18 Years to 85 Years with familial adenomatous polyposis who have undergone subtotal colectomy with ileorectal anastomosis, total colectomy with ileo-anal pull through (reservoir), and patients with intact colons with 5 or more adenomas in the rectum-sigmoid or reservoir. Experimental: Arm I (curcumin) Patients receive curcumin PO BID for 12 months. Laboratory Biomarker Analysis Placebo Comparator: Arm II (placebo) Patients receive placebo PO BID for 12 months. Laboratory Biomarker Analysis, outcome measure is Average number of polylys in the placebo arm at the end of the study is compared to the average in the curcumin arm.

**A Study Evaluating the Safety and Efficacy of Curcumin in Patients with Primary Sclerosing Cholangitis (PSC)**

The study involved 15 participants, having Primary Sclerosing Cholangitis Subjects will receive one 750 mg soft gel by mouth twice a day for 12 weeks. Each 750 mg CuraMed® soft gel supplies 500 mg of highly bioavailable BCM-95 curcumin.

**Intervention: Drug:** Curcumin Primary outcome - Change in Serum Alkaline Phosphatase (SAP)—Secondary outcome Change in Serum Aspartate Aminotransferase (AST), Change in Total Bilirubin, Change in C - reactive protein (CRP) Results are The score shows very slight upward slope over time in stable patients, but during the terminal phase it shows an acceleration in progression. The total score for the MFIS is the sum of the scores for the 21 items ranging from score of 0-84. Higher numbers indicate greater fatigue. Pruritus will be measured by the 5-D Itch Scale. The scores of each of the five domains are achieved separately and then summed together to obtain a total 5-D score. 5-D scores can potentially range between 5 (no pruritus) and 25 (most severe pruritus).

**Therapeutic application of Allicin**

**Allicin Induces Calcium and Mitochondrial Disregulation Causing Necrotic Death in Leishmania**

Allicin has shown antileishmanial activity invitro and in vivo. However the mechanism of action underlying its antiproliferative effect against Leishmania has been virtually unexplored. In this study author present the results obtained in L. infantum and a mechanistic basis is proposed. Leishmaniasis is a vectoral parasitic disease caused by flagellate organisms from the genus Leishmania.

The result shown by this study was that allicin, at sublethal concentrations (Ca.EC50), induced an elevation of intracellular Ca2+ levels. In most eukaryotic cells a major signalling function of this cation in the cytosolic compartment is played when its levels are elevated. In Leishmania Ca2+ is maintained at very low levels and the fine tuning of its intracellular levels is critical for cell homeostasis. The high levels of intracellular Ca2+ observed in Leishmania exposed to allicin probably came from intracellular calcium stores and particularly mitochondrion, since no variations in the plasma membrane permeability were found at least as assessed by SYTOX Green internalization. There is a tight connection between oxidative stress and intracellular Ca2+ in all organisms including Leishmania. Although ROS are present in normal cells playing a significant role as signalling messengers the over production is linked to oxidative stress, mitochondrial dysfunction and cell death.

This study concluded that allicin induces dysregulation of calcium homeostasis and oxidative stress, uncontrolled by the antioxidant defence of the cell, which leads to mitochondrial dysfunction and a bioenergetic catastrophe leading to cell necrosis and cell cycle arrest in the premycotic phase.
In this study garlic (Allium sativum) has been used as a food as well as a component of traditional medicine. Aged black garlic (ABG) is known to have various bioactivities. However, the effect of ABG on allergic response is almost unknown. In this study author investigated whether ABG can inhibit allergic action of EBG or BG10 may include multiple targets such as Lyn. Furthermore, BG10 dose dependently decreased the phosphorylation of Syk, but not Lyn. Moreover, BG10 completely blocked the formation of prostaglandin E2 and leukotriene B4 at ≥25 μg/mL. When the effect of BG10 on FcεRI receptor cascade was investigated, BG10 significantly inhibited the phosphorylation of Syk, but not Lyn. Furthermore, BG10 dose dependently decreased the phosphorylation of cytosolic phospholipase A2 (cPLA2) and 5-lipoxygenase (5-LO) as well as the expression of cyclooxygenase-2 (COX-2). Consistent with what has been mentioned earlier, BG10 also significantly inhibited the PCA reaction in mice. In conclusion, this study demonstrated that EBG or BG10 possesses anti-allergic functions in vitro and in vivo systems. Moreover, BG10 may be concentrated with anti-allergic components that are extracted from ABG, because BG10 has more potent anti-allergic action than EBG. These findings revealed a beneficial feature of EBG in IgE-induced allergic responses. The mechanisms for the anti-allergic action of EBG or BG10 may include multiple targets such as Syk, cPLA2, 5-LO, and COX-2. Such anti-allergic actions of EBG or BG10 may provide further information for the application of ABG preparation as functional food or a preventive agent.

**Antimicrobial properties of allicin from garlic**

This study shows us that allicin has verities of antimicrobial activities. Allicin in its pure form was found to exhibit antibacterial activity against a wide range of Gram-negative and Gram-positive bacteria, including multidrug-resistant enterotoxigenic strains of Escherichia coli; i)antifungal activity, particularly against Candida albicans; ii)antiparasitic activity, including some major human intestinal protozoan Parasites such as Entamoeba histolytica and Giardia lamblia; and iii)antiviral activity. The main antimicrobial effect of allicin is due to its chemical reaction with thiol groups of various enzymes, e.g. alcohol dehydrogenase, thioredoxin reductase, and RNA polymerase, which can affect essential metabolism of cysteine proteinase activity involved in the virulence of Escherichia coli. This study confirmed the ability of allicin to react with a model thiol compound (L-cysteine) to form the S-thiolation product, S-allyl cap to cysteine. The identification of the thiolation product was proven by nuclear magnetic resonance as well as by mass spectroscopy. In conclusion study showed, that the wide spectrum antimicrobial effects of allicin (and ajoene) are due to the multiple inhibitory effects they may have on various thiol dependent enzymatic systems. It is difficult at this stage to state which are the more lethal targets. It could very well be that the effect of allicin may be at different levels. Some enzymes such as the thiol proteases, which cause severe damage to the host tissues, may be inhibited at the lowest concentrations. At low concentrations the inhibition of these enzymes may not be lethal, but sufficient to block the microbe’s virulence. At slightly higher concentrations other enzymes such as the dehydrogenases or thioredoxin reductases may be affected, and even partial inhibition of these enzymes could be lethal for the microorganism. The wide range of biological activities that allicin has been found to have should have propelled this molecule into becoming a prime candidate for therapeutic use. Unfortunately, until now pharmaceutical companies have not become interested in investing in the development of this antimicrobial molecule as a drug and in performing the necessary preclinical and clinical efficacy trials.

**Antischistosomal and anti-inflammatory activity of garlic and allicin compared with that of praziquantel in vivo**

The main purpose of this study was to investigate the potential anti schistosomiasis and anti-inflammatory activity of both garlic extract and allicin on liver fibrotic markers in BALB/c mice with schistosomiasis (S.mansoni infection) compared with that of the commonly used drug, Praziquantel (PZQ).

The major conclusion of this study was that crushed garlic homogenate and allicin are potential complementary treatments that may be used with PZQ.

**Diallylthiosulfinate (Allicin), a Volatile Antimicrobial from Garlic (Allium sativum), kills Human Lung Pathogenic, Bacteria, Including MDR strains, as a vapour**

The main purpose of this study was to show how volatility of allicin makes it potentially useful for combating lung infections. Allicin was synthesized (>98% pure) by oxidation of diallyl disulphide by H2O2 using formic acid as a catalyst and the growth inhibitory effect of allicin vapour and allicin in solution to clinical isolates of lung pathogenic bacteria from the genera pseudomonas, streptococcus and staphylococcus, including multi-drug resistant (MDR) strains was demonstrated. Minimal inhibitory (MIC) and minimal bactericidal concentrations (MBC) were demonstrated and compared to clinical antibiotics using standard European committee on Antimicrobial susceptibility Testing (EUCAST) procedures. The cytotoxicity of allicin to human lung and colon epithelial and murine fibroblast cells was tested in vitro and shown to be ameliorated by glutathione (GSH). Similarly, the sensitivity of rat precision –cut lung slices (PLCS) to allicin was decreased by raising the (GSH) to the approximate blood plasma level of 1mM. Because allicin inhibited bacterial growth as a vapor, it could be used to combat bacterial lung infections via direct inhalation. Since there are no volatile antibiotics available to treat pulmonary infections, allicin, particularly at sublethal doses in combination with oral antibiotics, could make a valuable addition to currently available treatments. The conclusion of this study was allicin in the gas phase is antimicrobial towards the majority of pathogenic isolates tested, including antibiotic resistant strains. However the relatively low differential sensitivity to allicin in vitro between animal and bacterial cells in liquid culture suggests that allicin alone may not be a suitable alternative to conventional antibiotics to treat lung infections, although the ameliorating effect of continual GSH supply to lung cells in vivo is an unknown variable. Nevertheless, in light of the historical precedents and increasingly urgent need for new alternatives, the use of allicin at sublethal doses in combination with other antibiotics merits further investigation.
Effects Of Allicin on Cardiovascular Risk Factors in Spontaneously Hypertensive Rats

The purpose of this study was to show the effects of purified allicin on the cardiovascular system and also the main aim of this study was to evaluate the effect of Allicin on blood pressure and triglycerides in spontaneously hypertensive rats. Allium sativum, the active ingredient in garlic, is known to have a beneficial effect on major cardiovascular risk factors, including dyslipidaemia, blood pressure, blood glucose and insulin levels. However, the data on the significance of these effects are inconsistent due to methodological limitations, especially the use of whole garlic cloves which does not allow controlled dosing of the active compound. The fact that in our present study, weight, insulin and adiponectin did not change raises the question whether allicin acts in more than one mechanism: in a dysmetabolic milieu allicin acts through its effects on weight and metabolic pathways; in a nondysmetabolic milieu, such as the conditions in our experiments, it acts through other pathways. The exact mechanism by which allicin exerts its biological action has not yet been fully elucidated. However, in this study there is the limitation that this study was unable to measure plasma levels of allicin, thus the correlation with the effects of allicin cannot be ascertained and in future research in vivo measurements of allicin and its physiological effects and mechanisms of action should be investigated further.


This study shows garlic and garlic extracts, through their antioxidant activities, have been reported to provide protection against free radical damage in the body. This study investigated antioxidant properties of garlic compounds representing the four main chemical classes, alliin, allyl cysteine, allyl disulphide, and allicin, prepared by chemical synthesis or purification. Alliin scavenged superoxide, while allyl cysteine and allyl disulphide did not react with superoxide. Allicin suppressed the formation of superoxide by the xanthine/xanthine oxidase system, probably via a thiol exchange mechanism. Alliin, allyl cysteine, and allyl disulphide all scavenged hydroxyl radicals; the rate constants calculated based on deoxyribose competitive assay were 1.4–1.7 1010, 2.1–2.2 109, and 0.7–1.5 1010M–1 second–1, respectively. Contrary to previous reports, allicin did not exhibit hydroxyl radical scavenging activity in this study. Alliin, allicin, and allyl cysteine did not prevent induced microsomal lipid peroxidation, but both alliin and allyl cysteine were hydroxyl scavengers, and allyl disulphide was a lipid peroxidation terminator. In summary, the findings of this study indicated that allyl disulphide, alliin, allicin, and allyl cysteine exhibit different patterns of antioxidant activities as protective compounds against free radical damage.

Effects of Allicin on Hypertension and Cardiac Function in Chronic Kidney Disease

This work was performed to study the effect of allicin on hypertension and cardiac function in a rat model of CKD. The groups were control (5/6nephrectomy), and CKD-allicin treated (CKDA) (40mg/kg/day/p.o.). Blood pressure was monitored (weekly/6 weeks). The cardiac function, vascular response to angiotensin II, oxidative stress, and heart morphometric parameters were determined. The CKD group showed hypertension and proteinuria. The coronary perfusion and left ventricular pressures were decreased in CKD group. In contrast, the vascular response to angiotensin II and expression of angiotensin II type 1 receptor (AT1R) were increased. These data were associated with the increment in morphometric parameters (weight of heart and left ventricle, heart/BW and left ventricular mass index, and wall thickness). Concurrently, the oxidative stress was increased and correlated inversely with the expression of Nrf2, Keap1, and antioxidant enzymes Nrf2-regulated. Allicin treatment attenuated hypertension and improved the renal and the cardiac dysfunctions; furthermore, it decreased the vascular reactivity to angiotensin II, AT1R overexpression, and preserved morphometric parameters. Allicin also downregulated Keap1 and increased Nrf2 expression, upregulated the antioxidant enzymes, and reduced oxidative stress. This study concluded that, allicin showed nephroprotective, antihypertensive, cardioprotective, and antioxidant effects, likely mediated by the downregulation of angiotensin II type 1 receptor and the Nrf2-inhibitor Keap1. Furthermore, our data provide evidence supporting the use of allicin as therapy in pathos physiological conditions in which cardiac and/or renal functions may be involved or associated.

Therapeutic Uses and Pharmacological Properties of Garlic, Shallot, and Their Biologically Active Compounds

Although allicin (diallyl-thiosulfate) is the most important alkaloid that is generally claimed to be responsible for their beneficial effects and numerous studies have been conducted so far, it is pointed out that other sulphur compounds such as diallyl disulphide (DDS), S-allyl cysteine (SAC) and diallyl trisulphide (DTS) also have some roles in the effects of the plant. In addition to A. sativum, A. tuberosum, A. hirtum, and other organo sulphides are present in A. Hirt folium and play important pharmacological roles.

However, care should be taken by scientists and clinicians regarding usage of this plant for therapeutic purposes until adequate studies confirm the safety and quality of the plant.

Finally based on this information, this review provides the evidence for other researchers to introduce garlic and shallots and their sole active compounds as safe and effective therapeutic sources in the future. In conclusion author stated that Garlic and shallots are safe and rich sources of biologically active compounds with low toxicity. Further studies are needed to confirm the safety and quality of the plants to be used by clinicians as therapeutic agents.
Clinical trials on Allicin

Identifying the Anti-Blood-Clotting Compounds in Garlic

ClinicalTrials.gov Identifier: NCT00200785

This study will seek to identify the compound(s) in garlic that is (are) responsible for its ability to prevent the formation of blood clots (prevent platelet aggregation) and to determine the maximally effective dose and duration of the benefits. This study will also determine whether "cooked" garlic (garlic powder added to boiling water, no allicin present) is as effective as "fresh" garlic (garlic powder added to ambient water, high allicin present) and, if more than one compound is involved, and whether their combined effects are more significant than the effects of each compound alone. Chronic studies. If only weak platelet effects are found for a high acute dose of "fresh" garlic, chronic studies will be conducted. In chronic studies, participants will consume 8.0 grams of "fresh garlic" (2.7 grams garlic powder added to ambient water, allicin content = 35 mg) as a paste in a tuna sandwich every day for four weeks and 8.0 grams of "boiled garlic" (2.7 grams garlic powder added to boiling water) in a sandwich every day for an additional four weeks, after a 1-week washout. The ability of platelets to aggregate in PRP and whole blood will be determined before and every week after garlic consumption begins and after the 1-week washout.

A Human Trial to Evaluate the Efficacy and Safety of Aged Garlic Powder on Improvement of Blood Lipids in Subjects with Hyperlipidaemia

ClinicalTrials.gov Identifier: NCT01402102

This study performed a double-blind parallel study in a group of mildly hypercholesterolemic subjects who were given aged garlic powder over a period of 12 weeks. We measured serum lipids, including total cholesterol, low-density-lipoprotein (LDL) and high-density-lipoprotein (HDL) cholesterol, and triglycerides, and monitored their blood pressure. An increased serum cholesterol level is an important risk factor for the development of cardiovascular and cerebrovascular disease. Reduction of these and other risk factors through dietary modification, behavioural changes, and medicinal intervention has already substantially decreased the incidence and mortality from cardiovascular and cerebrovascular disease. Supplementation of the diet with certain bifactors may further reduce such risk factors. Aged garlic belongs to a group of dietary supplements that may lessen the incidence of cardiovascular and cerebrovascular disease by reducing lipids levels and decreasing platelet responsiveness to activating agents

Effects of Garlic Supplements on Drug Metabolism

ClinicalTrials.gov Identifier: NCT00122889

This study will determine whether garlic supplements affect the way certain drugs are processed in the body Garlic supplements, which are often used to lower cholesterol and prevent cancer, are one of the most commonly used herbal products in the United States. However, little is known about the way garlic supplements may interact with prescription medications when used simultaneously. This study will investigate four commonly used garlic supplements: garlic powder with a low content of allicin (a compound with antibacterial properties), garlic powder with a high allicin content, garlic oil, and aged garlic. The effects of these 4 garlic products on the drug-metabolizing enzyme cytochrome P450 (CYP) and a drug transporter, P-glycoprotein (Pgp) will be examined. Participants will be randomly assigned to receive one of the four garlic supplements for 4 weeks. Drug probes of CYP and Pgp will be used to assess the in vivo activities of the substances. On the first day of garlic ingestion, blood collection will occur immediately after participants ingest their garlic supplement and 3, 4, and 6 hours after ingestion. Urine collection will occur immediately after participants' first garlic ingestion and 12, 15, and 72 hours after ingestion. Blood and urine collection will determine the concentration of the drug probes in the body, which will indicate changes in CYP and Pgp. Blood and urine tests will be repeated at the end of the study.

Allicin Bioavailability from Garlic Supplements and Garlic Foods

ClinicalTrials.gov Identifier: NCT00874666

This study will measure the bioavailability of allicin, the main active compound of garlic, from garlic supplements and garlic foods (raw, cooked, processed) so that supplement manufacturers and clinical investigators know how supplements need to be made and consumed to obtain high bioavailability consumers can know how garlic can be prepared to obtain any established health benefits of garlic. The bioavailability of allicin, the main active compound of garlic, from garlic supplements and garlic foods is highly questionable and unpredictable from in vitro tests, due to dependence upon alliinase activity under conditions that challenge alliinase activity (heat, gastric acid, intestinal proteases). It is likely that garlic supplement manufacturing procedures and coatings, meal conditions when supplements are consumed (high or low protein), and garlic food preparation conditions (temperature, surface area) will greatly affect allicin bioavailability. Such variability may account for some of the many conflicts seen in clinical trials on cardiovascular disease risk factors. To resolve these issues, this study will determine the actual bioavailability of allicin from several types of garlic supplements and garlic foods under various conditions. Bioavailability will be determined by measuring the area under the 32-hour curve for breath concentrations of allyl methyl sulphide, the main metabolite allicin.

Garlic in Hyperlipidaemia Caused by HAART

ClinicalTrials.gov Identifier: NCT 00029250

The purpose of this study is to test the effectiveness and tolerability of garlic pills in lowering cholesterol and triglycerides in hyperlipidaemic HIV-infected individuals who are being treated with highly active antiretroviral therapy (HAART). Clinical evaluation of garlic in HIV disease is warranted for several reasons. First, garlic is used as a botanical medicine and as an alternative therapy by many HIV-infected individuals. Baseline data from the Basty’s Alternative Medicine Care Outcomes in AIDS (AMCOA) study [1] indicate that garlic is the most frequently used botanical medicine among HIV-infected men and women (52.9%) who utilize complementary and alternative medicine (CAM). In the same cohort, 50% of the subjects who use antiretroviral therapy are also taking garlic supplements. Second, there is a growing body of studies that
indicate that garlic exhibits lipid and glucose lowering as well as hepato-protective activities. Third, several of the pharmacological activities of garlic and their reported clinical benefits in other conditions, especially in hyperlipidaemia, may be relevant in the management of highly active antiretroviral therapy (HAART) in HIV-infected subjects.

Study Medication: We will utilize GarlicinTM, an allicin-standardized dried garlic supplement in two escalating doses in HIV-infected subjects who are receiving HAART.

6. Effect of Aged Garlic Extract on Atherosclerosis (Garlic4)

ClinicalTrials.gov Identifier: NCT01534910

The investigators will be assessing the effect of Aged Garlic Extract on the coronary arteries. The investigators will enrol patients in a double blind study, where half the patients will receive placebo, and have the patients undergo a series of tests of plaque (CT scan of the heart, carotid ultrasound) and follow the patients on the drug or placebo and then repeat the tests and blood work at the end of one year. The investigators will assess if being on aged garlic extract adds any benefit to plaque in the coronary or neck arteries. The investigators will also assess the effect of aged garlic extract on markers of inflammation. Patients will receive free drug, free testing and be compensated, and learn more about their heart and neck arteries. If successful, more patients can use this drug to benefit their health. The harms include the radiation from the CT scan and the medication, which has mild side effects.

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Garlic Intake and Biomarkers of Cancer Risk

ClinicalTrials.gov Identifier: NCT01293591

This study is being done to study the healthy benefits of eating garlic. Previous studies suggest that garlic may help prevent cancer. The investigators are recruiting healthy volunteers to participate in a study to determine the ways in which eating garlic may reduce cancer risk. A crossover design will be utilized with each participant completing each treatment phase; participants will be randomly assigned to a sequence of dietary treatments. There will be a 17-day washout period in between diet periods. Participants will consume a garlic-free diet for the first 10 days of each diet period. The dietary treatments will be administered on day 11 of each diet period. Dietary treatments will be incorporated into food as follows: 1) 5 g (0.175 oz.) of garlic mixed with 15 g margarine on top of 270 kcal white bread, served as breakfast, or 2) 15 g margarine on top of 270 kcal white bread, served as breakfast.

Effect of Aqueous Extract of Garlic and Nystatin Mouthwash in Denture Stomatitis

ClinicalTrials.gov Identifier: NCT01198223

The aim of the present study was to compare the effect of aqueous extract of garlic with nystatin mouthwash in denture stomatitis, Denture stomatitis is the most common form of chronic oral candidiasis manifested as chronic inflammation of the mucous membrane supporting the movable prosthesis that may have a local or systemic nature. This inflammation is presented as mucous erythema and occasionally with pain and burning. The standard treatment for denture stomatitis is administration of nystatin which is accompanied with complications such as bitter taste as well as the high number of drug application that result in reduced tendency of patients in using this medication hence, efforts are continuously being made to substitute other types of therapies for this condition.

Conclusion

Chemical and in vitro cell studies have shown preventive properties of these compounds, being a potent antioxidant, against a variety of ROS and RNS. In addition, the epidemiologic and immunopathological studies suggest that consumption of these compounds may lower multiple disease risk. Such potential benefits have been ascribed in part to high concentrations of compounds in nutraceutical treatments. However, these findings have yet only been supported by a small number of intervention trials. By defining the right population and combining antioxidant and immunopathological potentials of these compounds with vitamins and other bioactive plant compounds, the beneficial role of them in other diseases that could be better clarified in future studies.

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