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RESEARCH ARTICLE

THE ROLE OF *ALLIUM SATIVUM* (GARLIC) IN VARIOUS DISEASES AND ITS HEALTH BENEFITS: A COMPREHENSIVE REVIEW.

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Abstract

Garlic belongs to the family Alliaceae, it has more than 500 species in 30 genera and the family is taxonomically intermediate between the Liliaceae and the Amaryllidaceae. It is widely distributed. *Garlic* contains more than one hundred biologically useful secondary metabolites, which include alliin, alliinase, alliin, S-allyl cysteine (SAC), diallyldisulphide (DADS), diallyltrisulphide (DATS) and methyl allyl trisulphide. The γ -glutamyl-S-alk(en)yl-L-cysteines are the primary sulfur compounds present in garlic. These active compounds are responsible for protection of tissue from damage and various disorders.

The therapeutic potential of this plant product inhibits invasion of carcinoma, provides cardiovascular protection, lowering of cholesterol and blood pressure, anti-platelet activities, and thromboxane formation. In addition the biological activities of garlic include antibacterial, antithrombotic, antioxidant, immunomodulatory, antidiabetic and modulation of drug metabolism. The other proposed uses of garlic include hepatoprotection, antihelminthics, antiinflammation, antifungal and wound healing. Based on our review, garlic based different ailments and concoctions can be used to alleviate a variety of health problems. Its various chemical and biological constituents contain different concentrations of organosulfur compounds to cure many diseases. Several researchers have provided a mechanism of action for many of their therapeutic effects.

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Introduction:-

Taxonomy:-

Kingdom : Plantae
 Division : Angiosperms
 Class: Monocotyledoneae
 Order: Asparagales
 Family : Alliaceae or Liliaceae
 Genus : Allium
 Species: sativum Linn

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Common Names:-

Garlic, Lasuna, Rasonam, Lasan, Vellulli, Vallai-pundu, Seer, Ullippoindu, Maharu

Geographical Distribution:-

Garlic is known in different names such as stinking rose, rustic treacle, poor man's treacle, *Allium sativum*, camphor of the poor, maidenhair tree and nectar of the Gods.

The Liliaceae family has more than 500 species in 30 genera and the family is taxonomically intermediate between the Liilaceae and the Amaryllidaceae. It is widely distributed and the major places of distribution for the whole family are Europe, Asia, North and South America.

Garlic is a bulbous variety of plant strong with pungent odour especially when crushed. The inflorescence is umbellate, small bulbils are produced in the inflorescences. The flowers are variable in number and sometimes absent, seldom open and may wither in the bud. Seeds are rarely produced. It occurs as entire bulb or isolated cloves (bulblets), bulb sub-globular, 4-6 cm in diameter, consisting of 8-20 cloves, surrounded by 3-5 whitish papery membranous scales attached to a short, disc-like woody stem having numerous, wiry rootlets on the under side. The odour is peculiarly pungent and disagreeable, acrid in taste and gives warmth to the tongue.

Chemical Compounds:-

There are more than two hundred chemical compounds in the Garlic bulb, of which, contains volatile oil with sulfur containing compounds abundantly like Ajoene (4,5,9-trithiadodeca-1,6,11-triene-9-oxide), Alliin and Allicin, enzymes like peroxidase, allinase, myrosinase and other compounds like α -phellandrene, β - phellandrene, linalool, citral and geraniol. (Eiaz *et al.*, 2003). Garlic contains at least 33 sulfur compounds and minerals like germanium, calcium, copper, iron, potassium, magnesium, selenium and zinc; vitamins A, B₁ and C, fibre and water (Gebreselema and Mebrahtu 2013). It also contains 17 amino acids like lysine, histidine, arginine, aspartic acid, threonine, swine, glutamine, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tryptophan and phenylalanine (Josling, 2005). The γ -glutamyl-S-alk(en)yl-L-cysteines are the primary sulfur compounds in the intact garlic, which can be hydrolyzed and oxidized to yield S-alkyl(en) yl-L-cysteine sulfoxide (alliin). Allicin is highly unstable and instantly decomposed to form various oil-soluble compounds involving diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS), vinyl dithiin and ajoene if conditions are appropriate (Brodnitz *et al.*, 1971). These active compounds are mainly responsible for protecting the tissue from damage and various disorders (Augusti 1996).

Water-soluble organosulfur compounds are odorless and possess more delicate and less characteristic flavor compared to the oil-soluble organosulfur compounds. Some researches have shown the reducing effect of garlic on HMG-CoA reductase in the cholesterol biosynthesis pathway (Gebhardt and Beck, 1996)

Medicinal and Therapeutic Uses:-

Garlic (*Allium sativum*) belongs to the family Liliaceae and it is also called as Poor Man's Treacle. Garlic is a traditionally cultivated plant which is widely used in culinary foods and utilized as a folklore medicine throughout human history (Hunter *et al.*, 2005). Garlic is used in medicines and foodstuff for almost three thousand years as evidenced by ancient writings from China, Egypt, Greece, and India (Cardelle-Cobas *et al.*, 2010) (Table 1). Garlic is an ayurvedic herb that has been extensively used as medication and as the taste enhancer of the food. Garlic has been reported to possess therapeutic properties, and is probably the most widely used medicinal plant in traditional system (Nrashan *et al.*, 2010).

Table 1:- Uses of garlic plant for treatment of different diseases

Parts of garlic	Preparation/aliment	Treatment
Leaves	Hot concoction	Common cold
Leaves	Tea	Reduce serum total cholesterol and triglyceride levels
Leaves	Oil	Blood thinning
Bulbs green	Crushed paste	Reduce platelet aggregation, hyperlipidemia
Bulb	Sticky juice	Adhesive in mending glass and porcelain

Bulb	Solvent extract(w/v)	Nematicide and insecticide for cabbage root fly and red mite in poultry
Bulb	Luke warm paste	Antiseptic to prevent gangrene
Crushed bulbs and dry stem	Folk medicine	Relieving pain, defense against malaria, flu, cold and sneezing deterring animals such as birds, insects and worms from eating the plant
Cherokee	Hot syrup	Expectorant for coughs and croup
Garlic+cinnamon	Bulb and bark mixture	Fish and meat preservative and antimicrobial
Total plant	Spiritual and religious	Both good and evil
Bulbs	In Europe	White magic

Source: Ravi Kant Upadhyay. 2016(10)1:1-28

Garlic bulb contains water (65%), carbohydrates (28%), organosulfur compounds (2.3%), proteins (mostly allinase; 2%), amino acids (1.2%) and fiber (1.5%) (Blumenthal *et al.*, 2000) Potential health benefits of vegetables, in particular garlic (*Allium sativum*), has its origin in antiquity, but still there is a need to unveil the details of benefits (Lewis and Elvin 2003).

It is used as medicine in the treatment of heart diseases, tumours, headaches and exhibits medicinal properties including immunomodulation, hepatoprotection, antioxidant, antimutagenic, antibacterial and anticarcinogenic effects (Agarwal 1996). Moreover, it has also been reported to possess antifungal (Halliwell *et al.*, 1992), hypoglycemic (Yoshida *et al.*, 1987), hypolipidemic, anti-atherosclerotic properties (Bordia, 1981) antidiabetic, antithrombotic, and antihypertensive, (Banerjee and Maulik 2002) and has been claimed to be effective against a number of diseases (Block *et al.*, 1984) (Table 2).

Table 2:- The medicinal Spectra of Garlic compounds

Pharmacologic Activity	Chemical Components of garlic contributed to activity
Anticoagulation	Ajoene
Antihypertensive	Selenium, germanium
Antimicrobial	Selenium, germanium
Antiparasitic	Allicin-alliin
Antibiotic	Allicin-alliin
Antimycotic	Allicin-alliin, Ajoene
Antiviral	Allicin- Ajoene
Hypolipemic	Diallyl disulfide
Detoxification of heavy metals	Selenium, allyl mercaptan germination
Antitumour	Selenium, germanium
Vitamins	Thiamine, vitamins A and C
Antioxidant	Selenium, germanium
Antiaging	Selenium, diallyl disulfide
Natural Killer Cell activity and other kinds of cell mediated immunity	Selenium, germanium
Humoural immunity	Germanium, allicin
Complement activity	Magnesium, Calcium

Source: Tariq *et al.*, 1988

On the other hand, garlic is an herbal medicine which is used for prevention and treatment of many diseases such as diabetes, thrombosis and hypertension. A health property of garlic depends upon the bioactive compounds especially

the organosulfur compounds (Rahman, 2007; (Tepe *et al.*, 2005), which are also responsible for the pungent flavor of garlic. Phenolic compounds are large groups of secondary metabolites that are able to neutralize or quench the free radicals (Picchi *et al.*, 2012). Flavonoids and their derivatives are the largest group of polyphenols found in plants (Hounsoume *et al.*, 2009).

Internal uses: Garlic is used to treat the following disorders.

Digestive system: Dysentery, diarrhoea, flatulence, indigestion, low appetite, colic pain, spasmolytic, constipation, worm infestation, piles, hepatitis and liver diseases

Endocrine disorders: Diabetes mellitus.

Skeletal system: Arthritis and rheumatism.

Circulatory system: Hypertension, arteriosclerosis, odema due to circulatory disorders, and diuretic.

Respiratory system: Chronic cough, expectorant, asthma, whooping cough, tuberculosis, bronchitis, allergies, lung diseases, sinusitis, tuberculosis, hoarseness of voice and pneumonia. Urinary system: urinary incontinence, urinary tract infections and kidney stones.

Anti fungal nature of garlic:-

In-vitro studies proved that garlic extract inhibited the growth of a large number of yeasts including *Candida* spp. and fungi such as *Coccidioides immitis* (Adetumbi *et al.*, 1986; Appleton & Tansey 1975; Barone & Tansey 1977;) and dermatophytic fungi *T. rubrum*, *T. mentagrophytes*, *T. verrucosum*, *Microsporum canis* and *Epidermophyton floccosum* (Aala *et al.*, 2010). Fresh aqueous garlic extract showed antifungal activity specifically against *A. fumigates*, *A. terreus*, *A. nidulans* and *A. niger* (Pai & Platt 1995). The activity of allicin against *Trichophyton* spp. is better than essential oils (biological compound) from *Allium* plants (Pyun & Shin 2006). Ajoene is an active compound found in garlic which plays a great role as topical antifungal agent. Garlic has been shown to inhibit growth of fungal diseases as equally as the drug ketoconazole, when tested on the fungi *Malassezia furfur*, *Candida albicans*, *Aspergillus*, *Cryptococcus*, *pencillium funiculosum*, *trichoderma brevicompactum* and other *Candida* species.

Antibacterial activity of garlic:-

The antimicrobial activity of garlic and garlic-derived organosulfur compounds was widely investigated against both food spoilage bacteria and food-borne pathogens (Leuschner and Ielsch 2003). Garlic inhibited the growth of 20 different strains of *Mycobacterium avium* intracellulare isolated from AIDS patients and non-AIDS patients (Deshpande *et al.*, 1993). Garlic extract inhibits the growth of Gram positive and Gram negative bacteria, such as *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Enterobacter*, *Escherichia*, *Klebsiella*, *Lactobacillus*, *Pseudomonas*, *Shigella*, *Salmonella*, *Proteus*, and *Helicobacter pylori* (Tsao and Yin 2001). Allicin's inhibits the growth of Gram positive *Bacillus* spp. *Streptococcus* spp. methicillin sensitive *Staphylococcus aureus* NBRC 12732 methicillin resistant *Staphylococcus aureus* (clinical isolates) Gram negative *Salmonella typhimurium* *Agrobacterium tumefaciens* *Escherichia coli* K12 *Pseudomonas syringae* (various pathovars) *Vibrio cholera* (Jan Borlinghaus *et al.*, 2014).

The antimicrobial effects of equivalent concentrations of garlic derivatives were seen in ground camel meat. The addition of either garlic or butylated hydroxyanisole (BHA) significantly delayed lipid oxidation when compared with the control. The antioxidant activities of the various ingredients added followed the order of fresh garlic (FG), garlic powder (GP), BHA, and garlic oil (GO) were studied. The results suggested that fresh garlic and garlic powder, through their combined antioxidant and antimicrobial effects, are potentially useful in preserving meat products (Hamid *et al.*, 2012).

Antimicrobial and Anti-proliferative activity:-

Garlic is nicknamed Russian penicillin for its widespread use as a topical and systemic antimicrobial agent (Agarwal 1996). The antimicrobial properties of garlic were first described by Pasteur (1958) by its activity against many species of bacteria, viruses, parasites, protozoan and fungi (Jaber and AlMossawi 2007).

Anti-proliferative activity of ajoene was demonstrated against a panel of human tumor cell lines (Li *et al.*, 2002). Supercritical CO₂ extraction of garlic oil is done to effectively extract heat sensitive, easily oxidisable, volatile substances like allicin which explore the inhibitory effect on human hepatoma HepG2 cell growth. Human hepatoma HepG2 cells were cultured in vitro, and changes in growth of allicin-treated HepG2 cells were determined by MTT assay and flow cytometry (Hailin *et al.*, 2016).

Anti Viral:-

Garlic and its sulfur constituents demonstrated antiviral activity against *Coxsackie virus spp*, *Herpes Simplex Virus types 1 & 2*, *Influenza B*, *Parainfluenza Virus type 3*, *Vaccinia Virus*, *Vesicular Stomatitis Virus*, *Human Immunodeficiency Virus type 1* and *Human Rhinovirus type 2*. The order for virucidal activity generally was: ajoene > allicin > allyl methyl thiosulfinate > methyl allyl thiosulfinate; no activity was found for the polar fractions, alliin, deoxyalliin, diallyl disulfide, or diallyl trisulfide. (Shoji *et al.*, 1993).

Ajoene, isolated from extracts of garlic may inhibit adhesive interaction and fusion of leukocytes (Tatarintsev *et al.*, 1992). Antiviral activity of garlic in humans may be secondary to a direct toxic effect on viruses. It also enhanced NK-cell (Natural killer-cell) activity that destroys virus-infected cells (Tariq *et al* 1988).

Antiparasitic and Anti-protozoal properties:-

Many folks healers and herbalists world wide recommend garlic as a treatment for intestinal parasites. In some cultures, children infested with helminths are treated with enemas containing crushed garlic (Weiss 1988). Allicin exhibits antiparasitic activity against major human intestinal parasites such as *Entamoeba histolytica*, *Ascaris lumbricoides* and *Giardia lamblia* (Ankri and Mirelman 1999). Many herbalists worldwide recommend garlic as a treatment for intestinal parasites (Pankaj Kashyap *et al.*, 2016).

Several studies have shown that the extract was effective against a host of protozoa including *Candida albicans* (Lemar *et al.*, 2002), *Scedosporium prolificans* (Davis *et al.*, 2003), *tinea pedis* (Ledezma *et al.*, 2000), *Opalina ranarum*, *Balantidium entozoon*, *Entamoeba histolytica*, *Trypanosomes*, *Leishmania*, *Leptomonas*, and *Crithidia* (Reuter *et al.*, 1966).

Antioxidant principle of garlic:-

The strong antioxidant effect of garlic extract has also recently been claimed to prevent cancer, thrombus formation, cardiovascular disease and some diseases. The antioxidant potential of garlic *in vivo* and *in vitro* has been proved (Jackson *et al.*, 2002). Biochemical studies have demonstrated that garlic extract (GE) acts as antioxidants to protect cells against reactive oxygen species (ROS) (Chung 2006). Some previous studies have shown that garlic extract or some of its components may have potential anti-aging effects (Powolny *et al.*, 2011). The antioxidant effect of garlic and aged black garlic was studied in animals. The antioxidant activity of garlic and aged black garlic was measured as the activity in scavenging free radicals by the trolox equivalent antioxidant capacity (TEAC) assay. Consumption of aged black garlic significantly decreased hepatic thiobarbituric acid reactive substances (TBARS) level. The SOD, GSH-Px, CAT) activity of aged black garlic group was increased (Young-Min *et al.*, 2009). Aged black garlic recently available on the market in Korea is one of the garlic products expected to have strong antioxidant capacity. It is produced by ageing whole garlic at high temperature (70°C) and high humidity (90% RH) (Jang *et al.*, 2008; Kang *et al.*, 2008).

Garlic extract showed 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity (Querioz *et al* 2009) and superoxide dismutase (SOD) activity *in vitro* (Jang *et al.*, 2008). *in vivo* in the generation of reactive oxygen species (ROS) by heavy metals, which initiates lipid peroxidation, thereby causing oxidative damage to critical macromolecules like proteins, DNA as well as cell damage/ death (Das *et al.*, 2001).The effect of coadministration of garlic and ezetimibe on biochemical factors and antioxidant activity in hypercholesterol mice were tested. The activity of SOD, CAT and GSH levels were markedly increased in garlic and ezetimibe and combination of garlic and ezetimibe groups compared with hypercholesterole mice (Abbas Mohammadi *et al.*, 2014).The effect of garlic on the liver phosphatidate phosphohydrolase (PAP) activity, plasma lipid levels, malondialdehyde (MDA) and plasma antioxidant in rats fed either by normal or high-lipogenic diet with or without garlic lipogenic diet, Results showed that garlic significantly reduced (TC, TG, LDL-C, VLDL-C, liver triglyceride, MDA and plasma antioxidant in garlic treated rats (Esfandiar Heidarian *et al.*, 2011).

The effect of Garlic Powder on feeding performance, digestibility, blood lipid profile, digestive organs and carcass cuts of broiler chickens was studied. COL, TG, HDL, LDL levels were determined. Results of this study showed that Garlic Powder had no significant effects on broilers weight gain, feed intake (FI), feed conversion ratio (FCR), carcass cuts, visceral organs. However, garlic powder decreased COL, TG, LDL and increased HDL levels compared to control birds. The dry matter (DM), crude protein (CP) and ether extract (EE) digestibility were improved by feeding Garlic powder (Kamal Jamal 2012). The effect of raw garlic on patients suffering from alcoholic liver disease was studied. Blood samples were collected and the liver disease was measured by the

activities of liver marker enzymes (AST, ALT, ALP, GGT and LDH) which were elevated in alcoholic patients. Increased lipid peroxidation in alcoholic patients was accompanied by decreased activities of SOD, CAT, GPx. significantly lowered the activities of liver marker enzymes (Sankaran Mirunalini *et al.*, 2010). Garlic extract exerts antioxidant action by scavenging reactive oxygen species ROS, enhancing the cellular antioxidant enzymes; SOD, CAT and Gper and increasing glutathione in the cells. Garlic inhibits lipid peroxidation, reducing ischemic/reperfusion damage and inhibiting oxidative modification of LDL. Garlic protects DNA against free radical-mediated damage and mutations (Carmia 2001). Gentamicin (GM) nephrotoxicity has been related to oxidative stress. Garlic and metformin (MF) have antioxidant activity and therefore, this study against curative effects of garlic, MF and their combination on GM induced tubular toxicity in Wistar rats was done. The results indicate that MF and garlic or their combination have curative and protective activity against GM nephrotoxicity.

Immunomodulatory effect of garlic:-

Garlic has probably been most popularized as a complementary therapy for blood pressure control, as it is used by approximately 50% of patients who have hypertension (Capraz *et al.*, 2006). Recent in vitro studies by Benavides *et al.*, (2007) have confirmed the vasoactive ability of garlic's sulfur compounds. Aged garlic extract contains the active and stable component S-allylcysteine, which allows standardization of dosage (Lawson and Gardner 2005) In isolated strips of canine carotid arteries and in isolated rat aorta, garlic exerted direct vasodilating effects (Ozturk *et al.*, 1994) Garlic also activates the synthesis of nitric oxide, which is a potent endogenous vasodilator (Das *et al.*, 1996).

The effects of processed garlic (PG) on the systolic blood pressure (SBP) and the diastolic blood pressure (DBP) of spontaneously hypertensive rats (SHR) and on the BP of hypertensive humans was significant, DBP reduction was also found in the placebo group, which might be attributed to a placebo effect. After 8 weeks, PG lowered SBP. In conclusion, it had significantly lowered blood pressure in hypertensive subjects (Chuan-Hsiao *et al.*, 2011).

Endothelial NOS (eNOS) derived NO induces relaxation of vascular smooth muscle cells leading to vasodilatation via guanylyl cyclase dependent mechanism (Forstermann and Sessa 2012). The antihypertensive properties of garlic have been linked to stimulation of intracellular nitric oxide and hydrogen sulphide production, and blockage of angiotensin II production, which in turn promote vasodilation and thus reduction in Blood Pressure (Castro *et al.*, 2010). The study was investigated the effect of consumption of garlic powder on blood pressure and renin angiotensin

system in a nitric oxide deficiency hypertension model in male rats. After different doses of injection of angiotensin I and angiotensin II, mean arterial pressure was significantly increased in the normotensive-garlic and the hypertensive-garlic groups, respectively Garlic powder consumption has reduced blood pressure, it did not have an effect on the interaction between renin angiotensin system and nitric oxide inhibition. (Aliasghar Vahidinia *et al.*, 2015).

Inhibitory effect on cardiac arrest:-

Garlic and its derived compound ajoene have demonstrated inhibition of platelet aggregation in vitro as well as in experimental animals and reduction of platelet dependent thrombus formation (Shah *et al.*, 2014). Studies have shown that garlic has great potential in inhibiting platelet aggregation and enhancing fibrinolytic activity (Sogani and Katoch 1981). Recent in vitro studies have confirmed the vasoactive ability of garlic's sulfur compounds, where by red blood cells convert garlic's organic polysulphides into hydrogen sulphide, a known endogenous cardioprotective vascular cell-signaling molecule (Benavides *et al.*, 2007).

Joshua Adamu *et al.*, 2014 investigated liver function profile, hematological and biochemical effects of garlic, the liver histology revealed evidence of distorted cyto-architecture of the liver cells in animals treated with combination of garlic. The hematological parameters were tested in rats fed by giving garlic as a juice for 30 days significantly, increased the red cell count, haemoglobin concentration and the PCV when compared with the control. Also garlic fed rat showed a significant increase in total white blood count, neutrophils, monocytes and the lymphocytes. No significant changes were observed in the basophil and eosinophil counts of animal fed with garlic, when compared with control (Iranloye 2002). The effect of feeding garlic powder (GP) on the performance, digestibility, digestive organs, carcass cuts and lipid profile of broilers Cobb-500 chicks were seen, Blood samples from 3 birds per replicate were collected on 3rd, 5th and 6th week post feeding from wing vein for blood lipid profile determination. COL, TG, HDL, low density lipoprotein (LDL) were determined. Results showed that GP had no significant effects on broilers weight gain, feed intake (FI), feed conversion ratio (FCR), carcasscuts, visceral organs. However, GP

decreased COL, TG, LDL and increased HDL levels compared to control birds. The dry matter (DM), crude protein (CP) and ether extract (EE) digestibility were improved by feeding GP (Kamal Jamal and Abo Omar 2012).

Anti cancer activity of garlic:-

The anticancer effect of diallyltrisulfide in human colon cancer cells HCT-15 and DLD-1 was due to disrupted microtubule network formation of the cells. There are several prognostic biomarkers like nuclear receptors whose over-expression is associated with Breast cancer characteristics. These biomarkers can be blocked by compounds with anti-cancer potential by the Docking studies and ADMET evaluation revealed twelve compounds to be active against the targets (Nabarun Roy *et al.*, 2016). The cytotoxic activities of the ethanolic extract of bulb of *Allium sativum* against human cancer cells was determined by SRB assay. A comparative study was done with two other Cell Line namely Central Nervous System Cell Line and Colon Cancer Cell Line. The cytotoxic activity shown by the ethanolic extract of *Allium sativum* against Colon cancer cell line was more when compared to that of CNS cell line. (Ekta Prakash *et al.*, 2016). The anti-proliferative effect of allicin was analysed on human hepatoma HepG2 cells using MTT assay and flow cytometry in order to provide data support for its clinical application. Allicin has a marked inhibitory effect on HepG2 cell growth; moreover HepG2 cell inhibition rate increases with increasing allicin concentration and treatment time (Hailin *et al.*, 2016).

The effect of garlic oil (GO), alone or combined with low dose total body gamma (γ)-irradiation (LDR) against paracetamol (APAP)-induced hepatotoxicity was investigated in rats. GO oral administration for 14 days, LDR irradiation for 2 hours were done prior to hepatotoxicity induction by peroral APAP administration. Then the rats were sacrificed 24 hours later. GO alone or combined with LDR, ameliorated APAP-induced adverse effects which was revealed by the reduction of serum liver marker enzymes activities and the histological examination. It could thus be concluded that the hepatoprotective activity of GO and LDR and their anti-oxidant and anti-apoptotic actions could be of beneficial value in the protective management of excessive hepatic damage induced by APAP hepatotoxicity. (Rasha *et al.*, 2014). Aged garlic extract (AGE), increases natural killer (NK) cell activity. In addition, animal studies have shown that AGE induces the release of cytokines such as IL-2, TNF- α and INF- α (Kyo *et al.*, 1998). These effects suggest that AGE, stimulates a Th1 cellular immune response that is characteristic of effective antitumor immunotherapies. Sundaram and Milner (1996) has reported that DADS was as effective as 5-fluorouracil (a potent anti-cancer drug) in inhibiting growth of tumors in transplanted human colon carcinoma cells.

Anti diabetic activity of garlic:-

The use of garlic as a folk medicine for diabetes has been reported in Europe (Mathew and Augusti, 1973) in India (Grover *et al.*, 2002) and in the Middle East (Bailey and Day 1989). Recent studies have directed their efforts towards the protective effects of plants such as garlic on hyperlipidemia (Ortega *et al.*, 2007). Garlic oil significantly decrease the levels of antioxidant ceruloplasmin, albumin and total thiols in the plasma of diabetic rats but SOD activities was decreased in tissue homogenates of liver and kidney (Mamdouh and Abdel-Raheim, 2003). Garlic has also been shown to have antioxidant properties, gastrointestinal neoplasias, against blood clots (anti-platelet action) due in part to the compounds alliin and ajoene, which have fibrinolytic activity (Metwally 2009) Most of the studies showed that garlic can reduce blood glucose level in diabetic mice and rabbits (Ohaeri, 2001) From a comparison study made between the action of garlic extract and glibenclamide, it was shown that the antidiabetic effect of the garlic was more effective than the glibenclamide (Eidi *et al.*, 2006). Aqueous extract of garlic (500 mg/kg/d IP) increased total serum antioxidant levels in STZ-treated diabetic rats.

Alloxan diabetic rats with the antioxidant SACS isolated from garlic, controlled lipid Peroxidation and stimulated in vitro insulin secretion from B cells isolated from normal rats (Augusti and Sheela 1996). Garlic extract attenuated hypoglycemia and structural nephropathy progression in streptozotocin (STZ)-induced diabetic rats (Al-Qattan *et al.*, 2008). Consumption of diet containing 5% garlic powder significantly decreased serum glucose and total cholesterol in db/db mice, an animal model of type 2 diabetes. The anti diabetic effects of garlic were studied in alloxan induced diabetic male rabbits, compared to normal control and diabetic control male rabbits. The serum cholesterol level and body weight were also studied. the significant hypoglycaemic, hypocholesterolaemic and hypolipidaemic effects were shown. Therefore, study reinforces the findings of previous studies that garlic had a significant effect in reducing blood glucose (Mahesar *et al.*, 2010) The hypoglycemic properties of the ethanolic extract of the bulbs of *Allium sativum* were evaluated in normoglycemic rats. The ethanolic extract of *A. sativum* bulbs reduced the blood glucose level after treatment in albino rats (Shakya *et al.*, 2010).

The potential immunomodulatory effect was shown by administration of allicin in the autoimmune disease process of type 1 diabetes the levels of anti- islet cell antibodies, Pan T lymphocytes marker (CD90), Pan B lymphocytes markers (CD19), and Pan innate cells marker (CD11b) were decreased in male rats with Streptozotocin-induced type 1 diabetes. The administration of allicin especially in high doses to the type1 diabetic rats leads to a significant decrease in the levels of all immunological parameters and stop the disease process (Muhamed Osman *et al.*, 2016). The effect of garlic extract and glibenclamide on biochemical parameters, enzyme activities, and reduced glutathione content in the liver as well as on pancreas tissue in alloxan-induced diabetic rats were studied. These results suggest the potential of garlic extract as histo protective against free-radical-associated diabetes damage, preserving the ability of insulin secretion, and show a concentration-dependent antidiabetic effect(Lilia Douaouya and Noureddine 2016).

Conclusion:-

This review is useful to increase advanced knowledge on garlic therapeutic effects and improve our future experimental and clinical research plans. Several studies conducted on garlic have showed many health benefits and traditional uses worldwide over the centuries. Although it is shown that garlic may have a significant clinical potential either in their own right or as adjuvant therapy in different disorders. Garlic synthesizes series of sulfur compounds which shows multiple biological activities at nutrition and therapeutic level. Garlic contains organosulfur compounds which show cardiovascular, lipid-lowering effects, anti-platelet, hepatoprotective, antioxidant, anti diabetic, anti hypertensive, antiproliferative, anticancer, antioxidant, anti fungal, antimicrobial activity, anti parasitic and anti protozoal etc. It is rich in antioxidants which help, destroy free radicals that can damage cell membranes and DNA.

Because of its active principles role on health, garlic is attracting the interest of nutritionists, medicos, industrialists and business people.

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