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HISTORICAL PERSPECTIVE OF LEAD POISONING AND THERAPEUTIC APPROACH OF GARLIC (*ALLIUM SATIVUM*) AGAINST VARIOUS HUMAN ALIMENTS

Veena Sharma* and Surabhi Gupta

Department of Bioscience and Biotechnology, Banasthali Vidyapith, Tonk - 304022, Rajasthan, India.

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Correspondence to Author:

Dr. Veena Sharma

Professor,
Department of Bioscience and
Biotechnology, Banasthali Vidyapith,
Tonk - 304022, Rajasthan, India.

E-mail: drvshs@gmail.com

ABSTRACT: Lead comes in a category of toxic heavy metal which acts as a pollutant when present in high concentration in the environment and cause severe effects on the human body. Due to its continuous use its level increases and serves as a serious threat for the society. Lungs and skin are the first organs which get affected by Lead toxicity. Lungs are the most important and sensitive part of human therefore the toxic effects of lead toxicity on lungs cause severe damage. Garlic (*Allium sativum*) with medicinal properties is being used for various human ailments since ancient times. Due to its anti-cancerous, antidiabetic, antimicrobial, antioxidant activities helps in reducing the lead toxicity in the lungs as well. Garlic is rich in many components such as sulphur compounds, amino acids, vitamins, protein, trace elements thereby making it a potent therapeutic agent. Since, the therapeutic properties of garlic has not been considered up to its best possible level against heavy metal toxicity therefore, this article presents the toxicity of Lead on lungs and medicinal properties of Garlic.

INTRODUCTION: The environment is made up of three elements: land, atmosphere, and water, into which humans, plants and microbes resides. There are several layers in the environment which include biosphere- refers to living things, atmosphere refers to the air, lithosphere refers to land, and hydrosphere refers to water, that function together in harmony^{1, 2, 3, 4}. Pollutants like inorganic ions, organometallic compounds, heavy metals, radioactive isotopes, gaseous pollutants, and nanoparticles have significantly damaged the environment.

There are several heavy metals which pollute the environment which are as follows: Titanium, Vanadium, Chromium, Manganese, Iron, Cobalt, Nickel, Copper, Zinc, Arsenic, Molybdenum, Silver, Cadmium, Tin, Platinum, Gold, Mercury and Lead⁵. Since the ancient times, these heavy metals were found in the earth crust.

Anthropogenic activities like: metal mining, smelting, metal-based industries, foundries, leaching of metal from various sources include excretion, livestock's, runoff, automobiles, road works, landfills, and waste dumps results in heavy metal pollution^{6, 7, 8}. Mitochondria, nuclei, cell membranes, lysosomes and enzymes have negative effects on them when they are exposed to heavy toxic metals. These metal ions interact with the DNA and nuclear proteins present in the organelle and cause apoptosis, DNA damage or carcinogenesis to the cell⁷.

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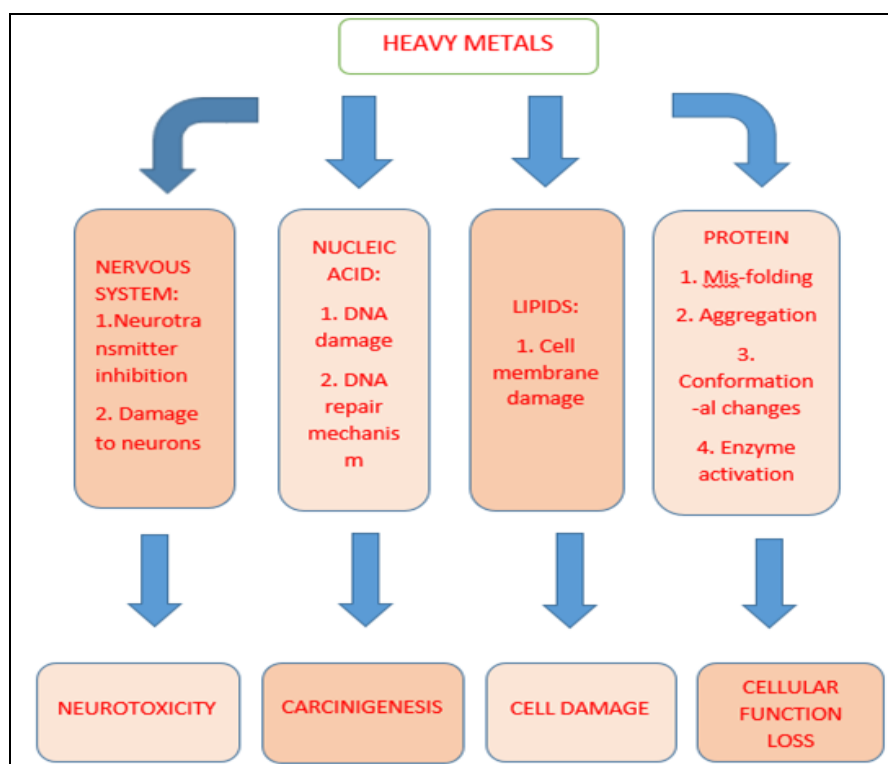


FIG. 1: EFFECTS OF HEAVY METALS (PICTURED BY SURABHI GUPTA AND DR. VEENA SHARMA)

Lead: Lead is one of the environmental contaminants, highly poisonous to living beings, absorbed mostly by respiratory system, digestive system and via skin too. Respiratory, urinary, cardiovascular and neurological diseases are caused by Lead exposure, as it affects the oxidative, immune-modulatory and inflammatory pathways^{9, 10}.

The sources of Lead exposure which we use in our day to day life are: lead based paints, cosmetics, gasoline, home dust, toys, polluted soil, and industrial erosion. Hence, recognizing the hazardous effects of Lead, its usage in many products such as paints, gasoline, and other such items has been drastically curtailed in recent years.

The amount of lead in skeleton muscles found to be 95% as insoluble phosphate and this determination was done by analysing the blood flow into the various tissues^{11, 12}. Lead toxicity can be acute or chronic, and the symptoms for the acute lead toxicity on their exposure are loss of appetite, headaches, hypertension, stomach discomfort, renal failure, exhaustion, insomnia, arthritis, hallucinations, and vertigo. These effects of Lead exposure were mainly found in the people working in manufacturing industries. There are some serious symptoms that shows lead can be fatal and even

can cause death to the humans, these symptoms are-mental retardation, birth defects, psychosis, autism, allergies, dyslexia, weight loss, hyperactivity, paralysis, muscle weakness, brain damage and kidney damage¹³.

Long term Lead exposure causes oxidative stress which result in several respiratory illness. These are: ischemia-reperfusion, chronic obstructive lung diseases, pulmonary fibrosis and asthma^{13, 14}. An antioxidant-oxidant imbalance between the Broncho-alveolar lavage fluid (BALF) and lung tissue cause respiratory illness^{13, 14}.

Recent studies gave the evidence that the incidence of asthma is inversely proportional to the consumption of antioxidant vitamins in children¹⁵. When compared to healthy people¹³ the level of ascorbate and alpha-tocopherol concentration was found to be low in asthma patients. Variations in the activity of several antioxidant enzymes, Glutathione (GSH) depletion, protein-bound sulfhydryl groups, are linked to lipid peroxidation.

Lead Properties: Lead is soft, greyish or silvery white metal in the group 14 (IVa) of the periodic table in chemistry. Pb is the symbol (abbreviation) of Lead. It is highly malleable¹⁶⁻²².

Atomic Number: 82

Melting point: 327.5 °C (621.5°F)

Atomic weight: 207.19

Density: 11.29gram/cm³

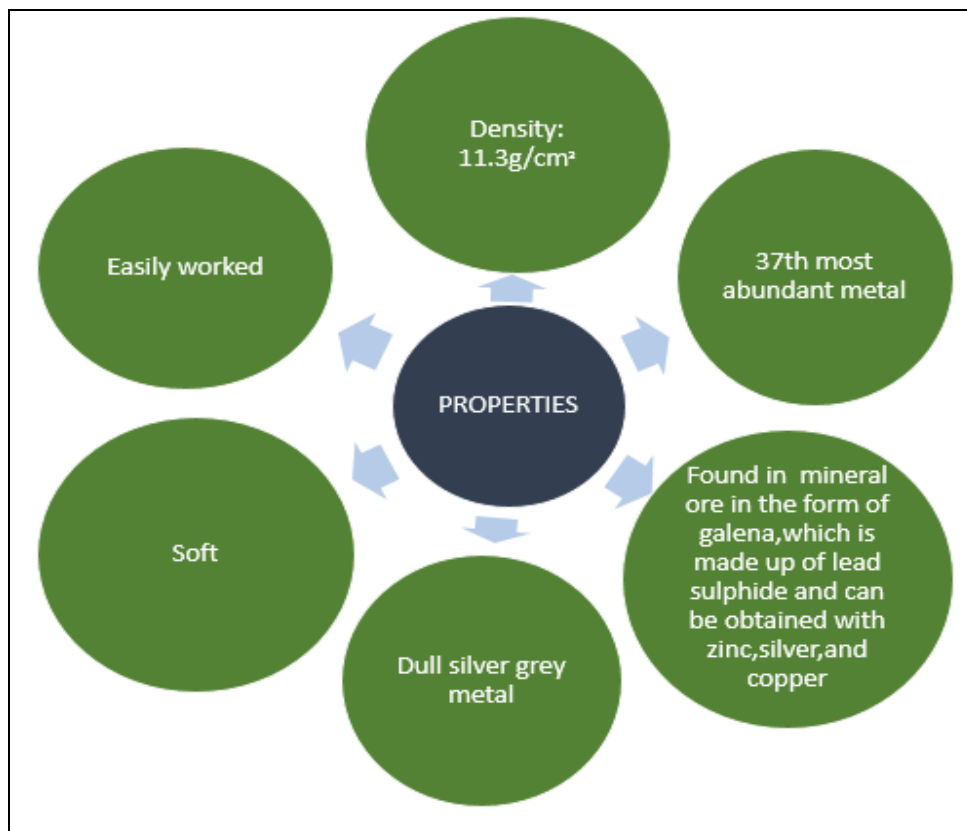


FIG. 2: GENERAL PROPERTIES OF LEAD (PICTURED BY SURABHI GUPTA AND DR. VEENA SHARMA)

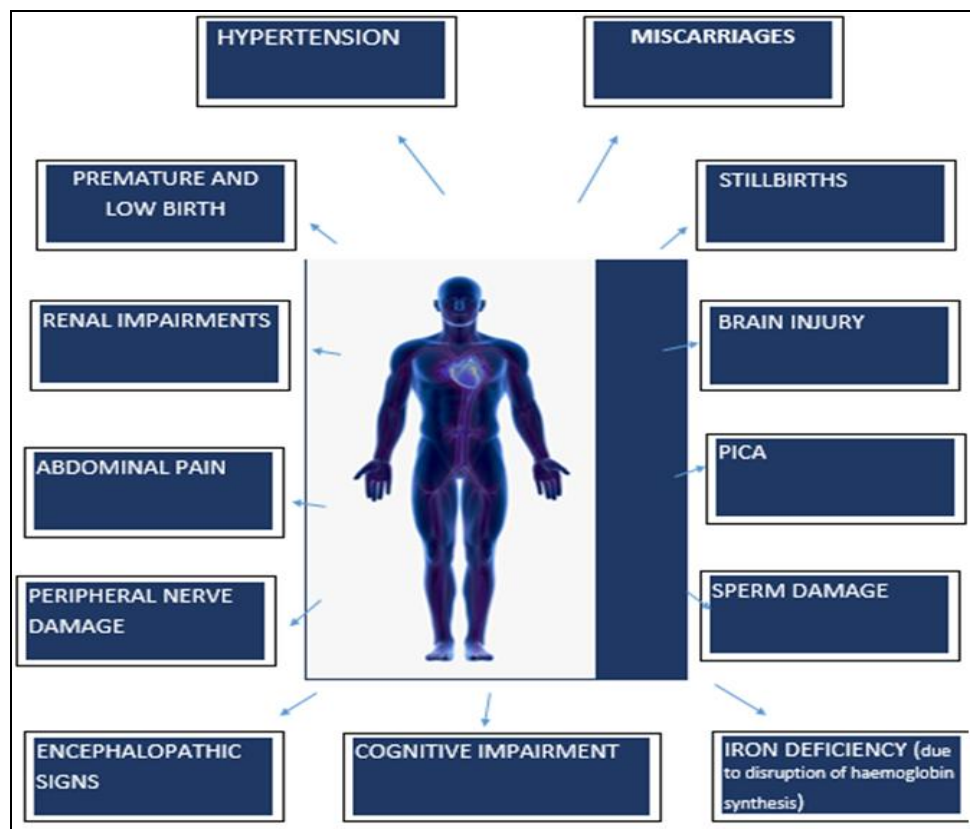


FIG. 3: EFFECT OF LEAD ON HUMAN BODY (PICTURED BY SURABHI GUPTA AND DR. VEENA SHARMA)

Uses of Lead: Lead has broad range of applications. It is used in car making, paints, in the finest crystal and optical glasses, shields against

nuclear radiation, making pencil, in mining, smelting, and refining, in storage batteries, grid, sheet, solder, babbi type metal and many others.

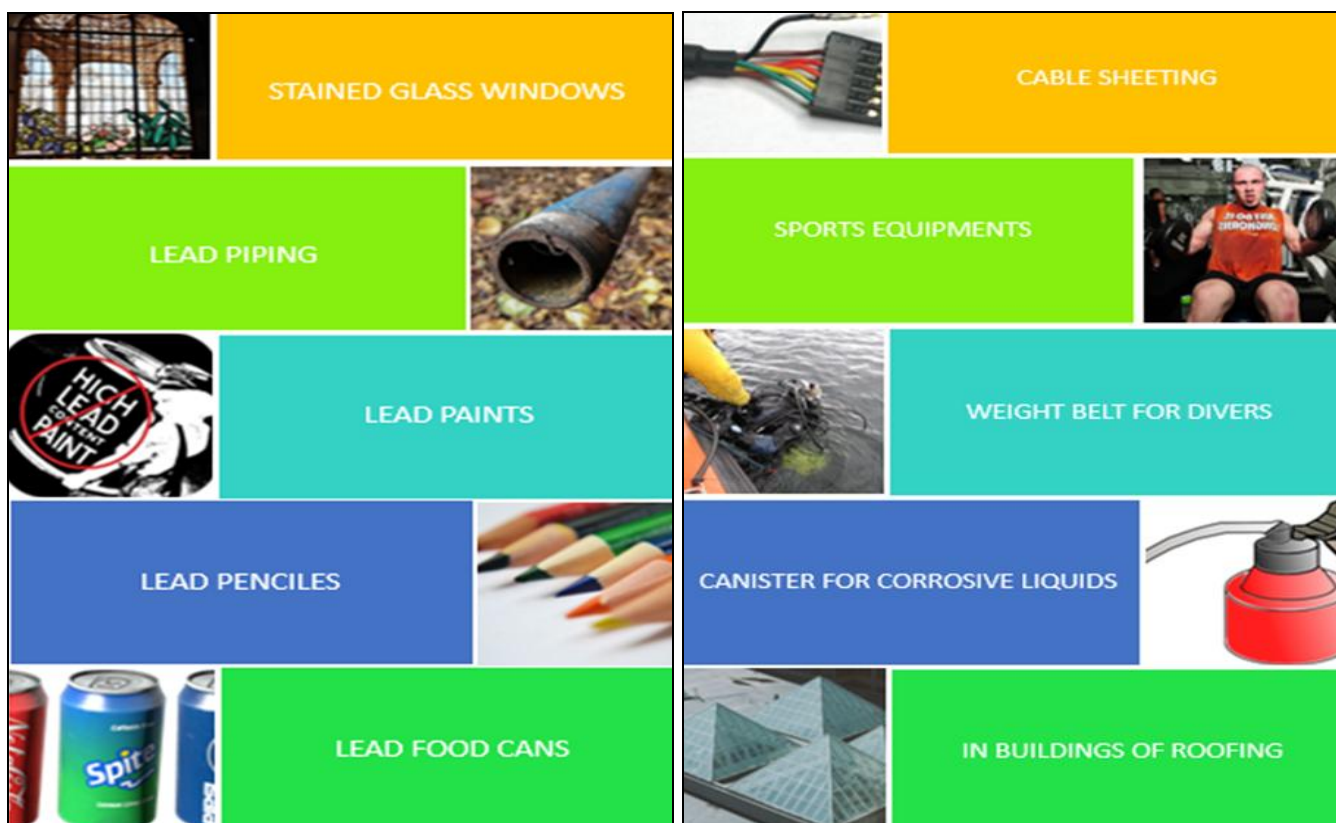


FIG. 4: USES OF LEAD ON DAY-TO-DAY LIFE (PICTURED BY SURABHI GUPTA AND DR. VEENA SHARMA)

Lead Toxicity: Lead enters into the body through the lungs by inhalation, by ingestion through intestine, through skin, or by swallowing. Inorganic lead absorption take place throughout the gastrointestinal and respiratory tracts. After the lead is absorbed, it accumulates into the three compartments: bones, soft tissues and blood. In blood approximately 99% of lead accumulates in erythrocytes, and remaining 1% in plasma and serum. Lead concentration in plasma (Usually below 1% of that in blood) is probably more relevant to lead toxicity and exposure^{23, 24}. Lead is toxic and its toxicity in living cell caused by oxidative stress and by several mechanism. An

oxidative stress against lead toxicity is the result of formation of imbalance between the antioxidants and free radicals in the cell such as glutathione. When exposed to lead there is an inverse relation between the reactive oxygen species and the amount of antioxidant, as one of them increases and the other decreases, mainly ROS increases while level of antioxidants decreases. A reaction mechanism in the case of glutathione, it occurs naturally as a reduced form *i.e.*, GSH in addition to its oxidised form *i.e.*, GSSG. Hence, in order to establish its stabilized form the reduced form of glutathione is observed to donate its $H^{++} e^{-}$ reduced equivalents to ROS.

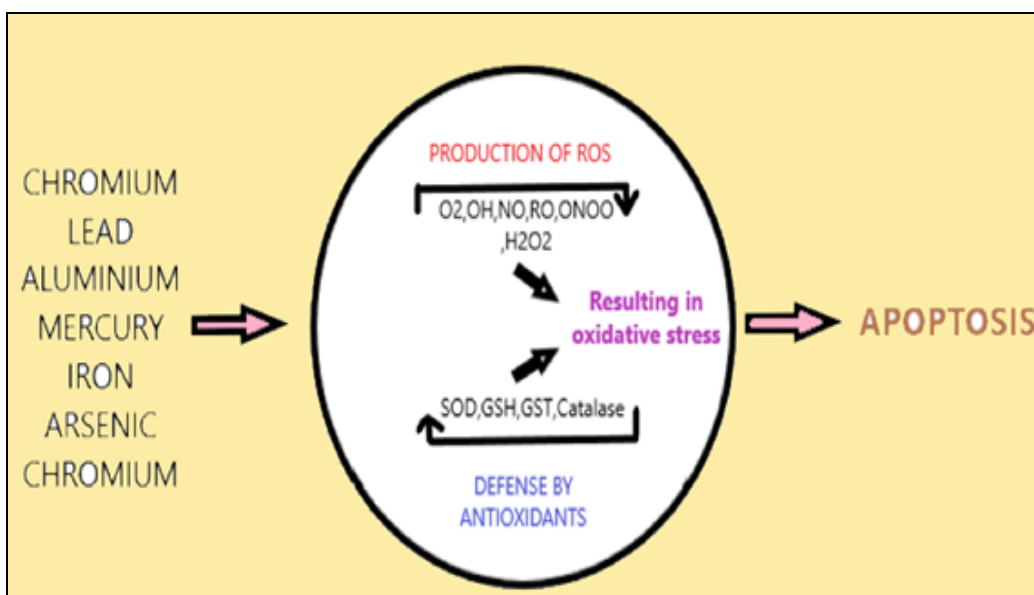


FIG. 5: HARMFUL EFFECT OF HEAVY TOXIC METALS ON THE CELL, SHOWING THE BALANCE BETWEEN THE PRODUCTION OF ROS AND THE DEFENSE BY ANTIOXIDANTS RESULTING IN OXIDATIVE STRESS OF THE CELL AND FINALLY APOPTOSIS (PICTURED BY SURABHI GUPTA AND DR. VEENA SHARMA)

Lead causes toxic effect on every organ of the body. Studies show that toxic effect of Lead on blood is higher than any other tissues like: renal, cardiovascular, reproductive, neurological, haematological, immunological and developmental systems. Various studies shows significant association between PbB and mortality²⁵. Health effects related with the Lead are:

Respiratory Effects: There are several associations which are observed between Blood-Lead levels (PbB) and decreased lung activity, symptoms of respiratory disease, increased bronchial hyperactivity, and respiratory diseases like: asthma and obstructive lung diseases.

Endocrine Effects: Studies have shown that exposure of lead in children and adults cause several negative effects on vitamin D level, thyroid functions, cortisol levels, and serum level of growth factors.

Musculoskeletal Effects: Several researches have shown that there is an increased marker of bone metabolism, adverse periodontal, dental effects and bone loss in adult and children.

Body Weight Effects: On exposure to lead several studies have shown the evidence of decreased body weight in children and adults²⁵.

Acute Lead Toxicity: The conditions of acute toxicity that is caused by lead is mainly observed by signs and symptoms such as swelling in the cerebral region, encephalopathy, peripheral neuropathy and vomiting leading to severe cases of coma, seizer as well as death of the patient.

Acute lead toxicity has a significant effect on the children as compared to the adults. Children are more prone to the lead toxicity as they have developing nervous system than adults who have fully developed nervous system²⁵.

Effect of Lead on Lungs:

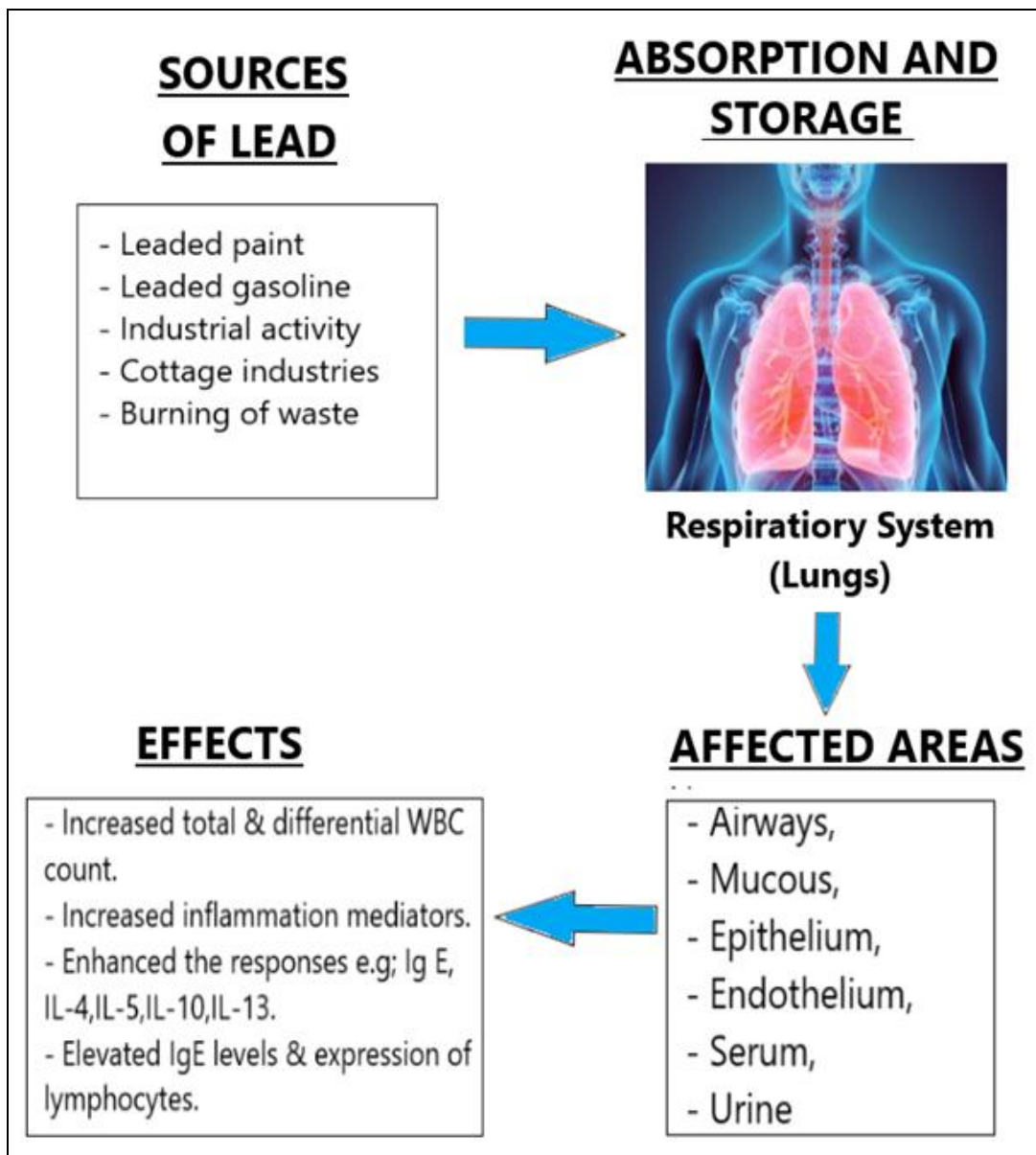


FIG. 6: EFFECT OF ENVIRONMENTAL LEAD ON LUNGS (PICTURED BY SURABHI GUPTA AND DR. VEENA SHARMA)

Lungs: Lungs are very important part of our body via which we breathe. They are situated on either side of the chest (thorax). They are spongy, air-filled organs. Lungs inhale air which is transferred to the tubular branches called bronchi, after that these bronchi divided into the smaller branches called bronchioles which in the end cluster together

as sac called alveoli, where exchange of oxygen and carbon dioxide occurs. Lung is surrounded with different layers as one of them is pleura, which is also present in the chest cavity. This layer helps the lung to contract and expand smoothly²⁶. Lungs are the sensitive part of our body. Heavy metals are main cause of the lungs malfunctioning.²⁷

There are many heavy metals present in the environment but the effect of Lead on lungs is high. It mimics the calcium activity in the human body as a result of which it causes toxicity in various organ. It affects several biochemical processes in the human body which includes calcium metabolism and carcinogenesis^{28, 29}.

Lung Toxicity with Respect to the Lead Exposure: Lead causes wide variety of the toxicities to the lung by several methods. These method include: inhibiting of enzyme activities, as a result of binding of the sulfhydryl group by changing the structure of cell membrane, receptors and by interacting with the proteins required for the cellular activities^{30, 31, 32}.

Garlic: Garlic (*Allium sativum*) is used as a table food worldwide. Garlic is often eaten raw, but it is also an essential ingredient, which is used to prepare many dishes³³. It has close relatives which includes Chinese onion, leek, chive, shallot, onion, Welsh onion. It is produced throughout the world but the 76% of it is produced by the China. Another name of garlic comes from the old English word garleac which means spear and leek as spear shaped leek.



FIG. 7: GARLIC (*ALLIUM SATIVUM*) (IMAGE CAPTURED BY SURABHI GUPTA)

It is an everlasting plant that grows from the bulb, it is tall, erect and flowering stem grows up to 1m. In Northern Hemisphere, in the month of July to September it produces flower of pink to purple colour. It produces 10 to 20 cloves which are asymmetrical in shape except those which are present in the centre^{34, 35}. Garlic has some important medicinal properties which include as: it lowers down the blood pressure level of the human

being, cholesterol level, fight with the several infections, and potentially prevent from the cancer. There are some sulphur containing compounds which are the active constituents present in it which are rapidly absorbed and metabolized. The bioactive components in garlic (*Allium sativum* L.) are responsible for its health benefits^{36, 37}.

Garlic History: Studies have shown that garlic has played an important role in food and therapeutic functions. Garlic is a gift from nature to humanity. Garlic is one of the important plant, which is used since the dawn of humanity as a culinary spice and medicinal herb. It is used since ancient times and used as medicine and food both by ancient scholars. Due to its medicinal and Ayurvedic properties, it has been used a popular remedy for various diseases and physiological disorders^{38, 39, 40, 41}. Medicinal plants have long been regarded as a gift from God to humans. It is also known as the first horticulture crops from the Old world.

Garlic Essential Oil: Essential oils are generally produced from the plant parts mainly from leaves, bulbs and bark. Essential oils are generally hydrophobic in nature as they are insoluble in water. They are less viscous with a specific odour and fragrance which leads them to be used in cosmetics and perfume industries.

Chemical Changes in Garlic: The chemistry of the garlic changes when it is dried, crushed, pulverised, exposed to water or acted upon the micro-organisms. When these conditions applied to the garlic the vacuolar enzyme allinase quickly lysed the cytosolic sulfoxides. Allinase converts the allin to allicin which break down into various chemicals like diallyl sulphide (DAS), diallyl disulphide (DADS), dithiins and ajoene quickly. Allicin, is a transiently produced chemical. Gamma glut amyl cysteine also converted to S-allyl cysteine (SAC) with another process, at the same time of allicin^{42, 43}. Garlic contains sulphur compounds, enzymes, amino acids, proteins, vitamins, trace elements and others;

A. Sulphur compounds⁴⁴ are as follows- alliin, allicin, ajoene, allyl-propyl disulphide, di-allyl tri-sulphide (DATS), S-allyl cysteine (SAC), vinyl-dithiins, S-allyl-mercapto-cysteine and others.

- B. Enzymes which are -Alliance, peroxidase, myrosinase, catalases, superoxide dismutase's, arginases, lipases.
- C. Amino acids which are -arginine, glutamic acid, aspartic acid, methionine, threonine.
- D. Proteins -glut amyl peptides.
- E. Vitamins-B1, B2, B6, C and E.
- F. Se, Ge, Te and other trace minerals.
- G. Biotin, nicotinic acid, elements, lipids, prostaglandins, fructan, pectin, adenosine^{45, 46}.

garlic which includes hydro- distillation, steam distillation, hot solvent extraction, and Soxhlet extractors. There are various preparative steps which needs to done before the extraction process. First the garlic should be properly peeled off, crushed, dried, paste like slurry should be made.

This is all according to the preference of the method adopted. Essential oil is very important in the human physiology and in the metabolism of organism and animals. Gas Chromatography and Mass Spectroscopy was performed to determine the various groups present in the garlic essential oil, according to their percentage yield.

Extraction of Garlic Essential Oil: There are several techniques to extract out the essential oil of

TABLE 1: GC-MS-DIFFERENT COMPONENTS PRESENT IN THE GARLIC OIL⁴⁷

Technique Used	Plant Part Used	Compound Name	Percentage
GC-MS	Garlic bulb	Diallyl di sulphide	68.09%
		Disulfide methyl propyl	52.34%
		Di sulphide methyl 2 propenyl	29.71%
		Sulphide allyl methyl	25.72%
		Di allyl sulfide	22.38%
		Di sulphide di methyl	9.88%
		(Z)-1- Methyl-3-(prop-1-en-1-yl)trisulfane	95%
		Trisulfide,methyl2-propenyl	95.55%
		(E)-1- Methyl-3-(prop-1-en-1-yl)trisulfane	65%
		Trisulfide, methyl 2- propenyl	95.55%
		3,4 Di-o-methyl-1-arabinopyranose	13%
		Trisulfide, di-2-propenyl	97.35%
		CH ₂ =CHCH ₂ SCH ₂ CN	13.3%
		(Z)-1-allyl-3-(prop-1-en-1-yl)trisulfane	37%

Garlic Properties: Garlic is known to have multiple medicinal properties which includes immune functions, antifungal, antibacterial, anti-virus, anti-oxidant, detoxification, inhibit platelet aggregation, lowering of cholesterol and triglycerides, reduction in blood pressure, anticancer effects, prevention of arteriosclerosis, and antithrombotic properties^{48, 49}.

Beneficial Role of Garlic:

Antioxidant: Garlic consists of many sulphur containing compounds which are used as a powerful antioxidant. Another key benefit of garlic for cancer patients is its capacity to fight against free radical damage. As garlic has medicinal properties, it inhibits the formation of the free radicals. It helps in elevation of antioxidant enzymes, which include superoxide dismutase, catalase, Glutathione peroxidase and inhibits the

activation of nuclear transcription factor kappa-B. It also help in the activation of the low-density lipoprotein from oxidation of free radicals. It also support endogenous radical scavenging mechanism^{50, 51, 52}. It also helps in reduction of radicals found in smoke of cigarette^{53, 54}.

Antimicrobial Activity of Garlic: Bacteria's are killed by antimicrobial activity of garlic. The antimicrobial effect of garlic juice was described by Louis Pasteur. Several studies have suggested garlic as an alternate therapy or prophylactic for infections, particularly gastrointestinal illnesses^{55, 56}. Being a traditional medicine, garlic has been used to treat viral, bacterial, fungal and parasitic illness. The therapeutic benefits, notably in terms of antibacterial capabilities, are attributed to allicin derived molecules, according to recent chemical characterisation of the sulphur component⁵⁷.

Allixin's antibacterial properties are attributed to its suppression of thiol-containing enzymes in microbes⁵⁸. Garlic's antimicrobial activity also showed action against some gram positive bacteria, gram negative bacteria (*Escherichia coli*, *Salmonella*, *Staphylococcus*, *Streptococcus*, *Klebsiella*, *Proteus*, *Bacillus*, and *Clostridium species*) and acid-fast bacteria like *Mycobacterium tuberculosis*^{59, 60}. Crush garlic cloves has allyl sulphides which was separated, identified as a responsible factor for antibacterial action^{61, 62, 63, 64}.

Anticancer Effect: Garlic also has the anticancer effect and it helps in the protection against some toxins which are hepato-toxins, cyclophosphamide, Adriamycin, methylcholanthrene, gentamicin, 4-nitroquinoline 1-oxide, and bromo-benzene shown by animal studies^{65, 66}. Due to its anticancer property it helps in inhibition of cancerous cells growth and proliferation by the presence of tumour promoter 12-O. Garlic can help in cancer prevention as per more recent research. Due to the cancerous effect the malignant cells form in the stomach and the liver, but the sulphurous components of the garlic prevents them from forming in them. On the basis of the studies, the exact mechanism of action is unknown while certain possibilities were taken into the consideration. Recently, two types of garlic was used the one, aged and the other fresh, the aged one has the strongest radical scavenging action and this property was shown by the two constituent present in the aged garlic which are; S-allyl cysteine and S-allylmercapto-L-cysteine. Garlic can affect carcinogen metabolism by either enhancing the activity of detoxifying enzyme systems that enhance the polarity of the carcinogen, allowing it to be excrete out from the body, or suppressing pro-carcinogen by activation of cytochrome P450. In phase II metabolism, glutathione-S-transferase is a detoxification enzyme.

Anti Covid Activity of Garlic: SARS-CoV-2 comes in the category of an enveloped virus and belongs to the family Corona-viridae. It induces IL-6, IL-1 and cause lung inflammation. It damage the organs of the host through expression of ACE2 (Angiotensin converting enzyme) receptor and cause imbalance between the renin-angiotensin system and ACE2/ angiotensin thereby enhance the infection/disease in organs.

Previous research showed that Garlic helps in reducing the symptoms of COVID-19 virus like shortness of breath and coughing, it also strengthens the lungs. Garlic organosulfur compounds also showed inhibitory effect against ACE2 protein *i.e.*, glycoproteins and PDB6LU7 protein. This study was performed by Molecular Docking simulation method. The results obtained proved that the virus entry into the host can be prevented as well as garlic essential oil help in activation of molecular pathway that restricts the discharge of pro-inflammatory cytokines. Protease (M^{pro}), is the main protease which plays essential role in replicating SARS-CoV-2. Garlic essential oils main component is Allixin which have the potential to constrain SARS-CoV-2 main protease by forming H-bond, and this inhibition also can be useful in treating COVID patients⁶⁷.

CONCLUSION: Lead act as dreadful toxicant if consumed in high concentration by the lungs and may cause severe problems in respiratory and other systems. In order to combat Lead toxicity, medicinal plants play significant role. Garlic is one of them, as it process various therapeutics agents which can overpower the harmful effects.

Significance of the Study: To the best extent this article provides historical perspective of Lead and focus light on the scope of *Allium sativum* as a therapeutic agent. The multiple constituents present in the garlic uplift the hope of researchers, that lung disorders caused by Lead intoxication can be minimized to a great extent.

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