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A Review on Phytoconstituents: Applications and its Role in Prevention of Disease, Cancer, and COVID-19

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Abstract:

Phytoconstituents are chemical compound which naturally occurs in plants. Some are responsible for color and other organoleptic properties. According to WHO (World Health Organization) more than 80 % world population is reliant on medicinal plants to maintain their health and to cure their abilities. The most important Phytoconstituents are alkaloids, terpenoids, phenols and phenolic glycosides, coumarins and their glycosides, flavones and flavonoid glycosides or heterosides, mucilages and gums, tannins, volatile oils, saponins, cardioactive glycosides, cyamogenic glycosides. Phytoconstituents play an important role in different categories like disease prevention, cancer prevention, and some of the Phytoconstituents play great role in prevention of COVID-19 such as curcuma longa(Turmeric), Zingiber officinale(Ginger), Cuminum Cyminum (Cumin), Allium Sativum (Garlic) and Piper nigrum(Black pepper). This review article represents the Phytoconstituents and their types, applications, functions, methods of extraction. Role of Phytoconstituents in different categories such as disease prevention, cancer prevention and in prevention of COVID-19. Some examples of Phytoconstituents such as curcuma longa(Turmeric), Zingiber officinale(Ginger), Cuminum Cyminum (Cumin), Allium sativum (Garlic) and Piper nigrum(Black pepper), Aloe barbadensis miller(Aloevera), Catharanthus roseus(Vinca).

Keywords: Phytoconstituents, Extraction, Evaluation, Function, COVID-19, Cancer, Turmeric, Ginger, Black pepper, Cumin, Garlic, Applications etc.

Introduction:

Phytochemicals are the nutritive chemical compound derived from plants, play a significant role in human disease prevention.[3] Natural products derived from medicinal plants with potent bioactive principles are the chief element of phyto medicine. They have versatile application in treating chronic as well as infectious disease. [2] Medicinal plants have played key role in world health. In the world 5-10% of all plants are systematically investigated for their medicinal property. Many of medicinal properties like analgesic, antitussive, antipyretic,

anticancer, antioxidant, antivenom, antimicrobial, antibacterial, antifungal, antitumour, antiulcerogenic, hypoprotective, cytoprotective, antidiarrheal, etc. [1] Phytochemicals which are naturally occurring compounds in plants foods are reported to provide various biological functions in humans. [4] It is now established and fully believed that Phytoconstituents obtained from the medicinal plants serve as pilot molecules in the modern medicines and many people still depend on the traditional medicine for their preliminary health care and treatment. [5] For the development of health in mankind the medicinal plants always play an important role. According to WHO (World Health Organization) more than 80 % world population is reliant on medicinal plants to maintain their health and to cure their abilities. [5] The most important Phytoconstituents are alkaloids, terpenoids, phenols and phenolic glycosides, coumarins and their glycosides, anthraquinones and their glycosides, flavons and flavonoid glycosides or heterosides, mucilages and gums, tannins, volatile oils, saponins, cardioactive glycosides, cyamogenic glycosides. [6]

Classification of Phytoconstituents:

1. **Phenolics**: Phenolics are plant metabolites widely spread throughout the plant kingdom. They are categorized as secondary metabolites. Recent interest in phenolic term from the potential protective role, through ingestion of fruits and vegetables. [7]
2. **Alkaloids**: Alkaloids are traditionally defined as basic, nitrogen containing organic constituents that occur mainly in plants. Emetine is an alkaloid of ipecac. [7]
3. **Saponins**: Saponins are phytochemicals found in most vegetables, beans and herbs. Saponins from Yucca and Quilaja are used in some beverages, such as beer, to produce stable foam. [7]
4. **Glycosides**: Glycosides are compound containing a carbohydrate and a non-carbohydrate residue in the same molecules. Non-sugar moiety is known as aglycone. Sugar moiety is known as glycone.[7]

Table 1: Classification of Glycosides:

Sr. No.	Types of Glycoside	Examples
1	Anthraquinones	Aloe, Rhubarb, Cascara, Senna, Frangula
2	Cardiac	Digitalis, squill, Quabain
3	Saponin	Discorea bark- Diosgenin, Ginseng- Gingenoside, Licorice- Glycyrrhizin
4	Coumarin and furocoumarin	Visnaga, Psoralea
5	Cyanophore	Wild Cherry, Bitter, almond
6	Isothiocynate	Black mustard
7	Phenol	Arbutin, Slicin

8	Aldehyde	Vanilla
9	Bitter	Gentian, Chirata, Picorrhiza, Quassia

5. **Terpenes**: The term 'Terpenes' was derived from terpentine. Terpenes are the hydrocarbons of plant origin of the general formula (C5H8) n as well as their oxygenated, hydrogenated and dehydrogenated derivatives. Thermal decomposition of Terpenes gives isoprene as one of the products. [7]
6. **Tannins**: The term tannins refer to the use of wood tannins from oak in tanning animal hides into leather; hence the word tan and tanning for the treatment of leather. [7]

   Classification of Tannins: Based on specific structural or characteristics and chemical properties -

   1. Gallotannins
   2. Ellagitannins
   3. Complex tannins
   4. Condensed tannins
7. **Anthraquinones**: Anthraquinones are a class of aromatic compounds with a 9,10-dioxoanthracene core. [7]
8. **Steroids**: Plants steroids are types of natural organic compounds found in plants. [7]
9. **Essential oils**: Essential oils are also known as volatile oils, ethereal oils, aethrolea or simply as the oil of the plants from which they were extracted, such as oil of clove. [7]

Method of Extraction of Medicinal Plants:

1. **Maceration**: The word maceration means softening. In this process the material to be extracted is placed in a closed vessel and suitable solvent is added and left for 7 days with occasional shaking. In case of vegetable and animal tissue, sufficiently long time is allowed for the menstrum to diffuse through the cell wall to solubilize the constituents present within the cells and for the resulting solution to diffuse out. [7]
   - **Types of Maceration**:
     1. **Modified Maceration**: Used for extracting unorganized drugs. E.g. Gums, resins. [7]
     2. **Multiple Maceration**: It is achieved maximum extraction by using portions of total volume of menstruum for successive maceration. Efficiently of extraction increases as the number of macerations increases. [7]
2. **Digestion**: The parts of the plants were introduced to extract in a container with the liquid preheated to the indicated temperature, maintained for a period that may vary between half an hour and 24 hours, shaking the container regularly. [7]
3. **Decoction**: The decoction is used for active ingredients that doesn't modify with temperature. In this process the plant is boiled in water for 15 to 60 minutes, it's cooled, strained and added enough cold water through the plant to obtained the desired volume. [7]

4. **Percolation**: Percolation depends upon the basic principle of diffusion for extraction; diffusion flows from a gradient of greater concentration to a lesser concentration. Percolation, however has the advantage of a continuous gravity driven flow of fresh, unsaturated solvent that works its way down through the marc. Since the soluble constituents are constantly wicked out of the marc by a less concentrated solvent the process can continue until the constituents are completely exhausted. [7]

Biological Function of Phytochemicals in Humans:

1. **Antioxidant functions**: Free radicals are continuously generated in the body by both physiological metabolism and disease status. Plants pigment phytochemical can be a part of our body defense system against oxidative stress, thereby reducing the risk of oxidative stress associated chronic status /disease such as inflammation. (e. g. Arthritis, cancer, cardiovascular and eye disease). There have been many reports concerning the relative antioxidant efficiency of phytochemicals, with varying results. As discussed above, the bioavailability of phytochemicals can be affected by various factors thus, their biological function including antioxidant activity. [4]
2. **Inflammation balance**: A recent randomized controlled multicenter trial indicated that dietary carotenoids. (Lutein, lycopenes and b- carotene) supplementation in preterm infants (n1/4 203) increases the plasma carotenoids concentration similar to human milk fed term infants and lower plasma C - reactive protein suggesting the anti- inflammatory effects of carotenoids. In addition, healthy men (n1/4 12/ group) consuming pigmented potatoes rich in carotenoids and flavonoid showed lower concentration of C-reactive protein and interleukin-6 as consuming men. The major effect of flavonoids on inflammation may be associated with the downregulation of the expression of proinflammatory markers, as has been recently received. [4]
3. **Cardiovascular health**: A recent review suggested a supplementation of low dose of lycopene as a preventive meas9for ameliorating cardiovascular disease. Among the fat-soluble plants pigment, lycopenes and astaxanthin have been proposed for their beneficial effects against cardiovascular disease. The antioxidant property of lycopene may be one of the mechanisms for its putative effects against coronary heart disease. However more evidence derived from well-designed clinical studies are required to provide stronger information about protective role of certain carotenoids against coronary heart disease. [4]
4. **Reducing the risk of cancer**: Epidemiological studies have consistently suggested that increased fruits and vegetables intake are associated with reduced risk of certain cancer. However, large-scale prospective studies are in consistent and recent systemic analysis even concluded that general increase in total fruit and vegetable intake had no impact on cancer rates in relatively well-nourished populations. There is modest evidence from human population studies that flavanols such as quercetin may reduce the risk of lung cancer. On the other hand, the lowa Woman's Health Study conducted in post-menopausal women showed an inverse association between catechins intake and rectal cancer incidence. A recent in vitro

study demonstrating the antagonistic effect of epigallocatechin gallate on androgen action suggests a possible inhibition of prostate cancer growth. [4]

5. **Neuro cognitive function**: The neurocognitive function of plant pigments phytochemicals has been described mainly in relation to the antioxidant functions. [4]
6. **Eye health**: Plants pigment in particular carotenoids have been extensively studied for potential preventive roles against age related macular degeneration and cataract through their blue light filtering and antioxidant functions. Flavonoids action for eye health have mainly been demonstrated in in vitro studies. Both epidemiological and laboratory data consistently indicate an association between oxygenated corotation of the retina and retinal pigment epithelium from damage by light and oxygen. [4]

Applications of Phytoconstituents:

Table 2 : **Applications of Phytochemicals in Pharmaceuticals**

Class of Phytoconstituents	**Phytoconstituents**	**Use of pharmaceuticals**
Terpenoids		
Monoterpene	Pinene, citronelol, limonene	Plant-plant interaction
Sesquiterpene	Abscisic acid	Plant growth hormones
Diterpene	Gibberellic acid	Plant growth hormone
Triterpene	Azadirachtin	Antifeedant, disruption of oviposition, reduction in fecundity
Phenolics		
Simple phenols	Catechol	Antifungal
Stilbenes	Resceratrol	Antifungal
Flavonoids	Quercetin	Pigmentation and defense
Polyphenols	Lignins	Blocking the pathogenic growth
Furanocoumarins	Umbelliferone	Fungal defense
Isoflavonoids	Naringenin	Promoting the formation of nitrogen fixing nodules by symbolic rhizobia
Nitrogen and sulfur containing compounds		
Alkaloids	Pyrrolizidine	Antimicrobial
Cynogenic glucosides	Amygdalin	Broad spectrum defense
Phytochelatins	Glutathione	Cellular antioxidant
Glucosinolates	Allyl-cys-sulfoxide	Antifungal

Dietary fiber		High-fiber diets may help prevent colon cancer and be used to treat constipation, diverticular disease , irritable bowel syndrome and Crohn's disease

Future Prospects of Phytochemicals in Pharmaceuticals:

In many countries, there is a fast use of medicinal plants. But only in the recent era have some of them been scientifically proven for nutritional and medicinal evidence. These are now being referred to as Phytoconstituents. The recent research interests focus on the relationship between the structure and function of the Phytoconstituents. Nowadays it has become important to recognize and purify the bioactive markers from the plant's sources. Recently the pharmaceutical industries have shown a significant interest to improve the medicinal property of natural foods by modifying the food habits of the consumers. The useful ingredients containing foods should be manufactured in the food industries and make them most popular to the people. The foods which are the choice for most people may not filled with markers and active constituents to control diseases. Many scientific data have superscripted the subsequent markets for phytochemicals in the use of pharmaceuticals. The usage of healthy ingredients which are not traditionally considered as nutrients is increasing extensively. [26]

Role of Phytoconstituents:

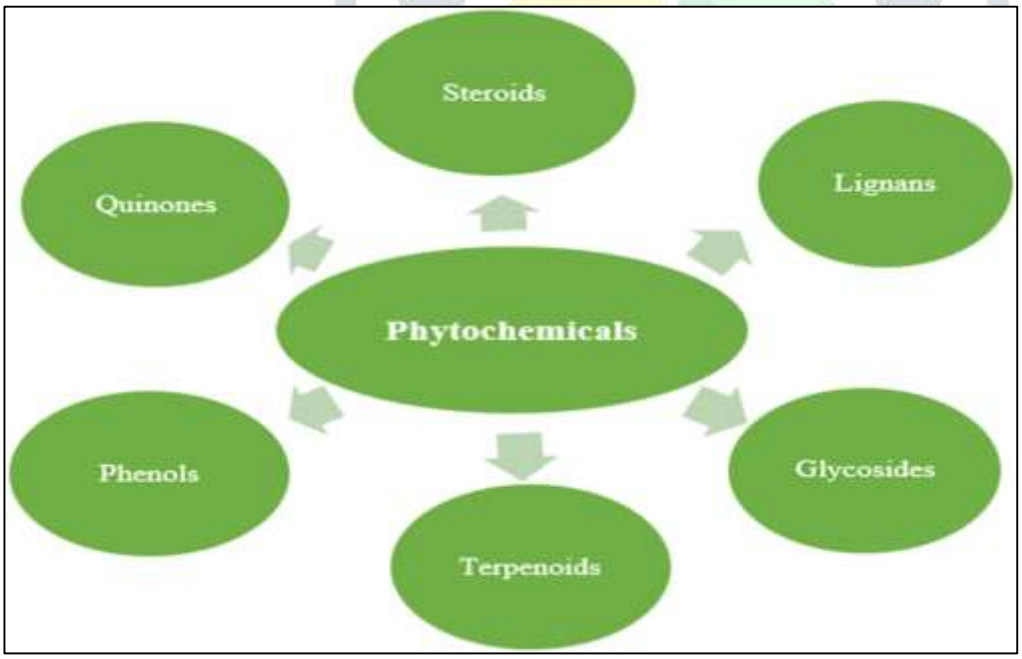

Figure 1 : Role of Phytochemicals

1. Role of Phytochemicals in Disease Prevention:

Phytochemicals present in medicinal plants, such as alkaloids, tannins, saponins, flavonoids, phenols, steroids, carotenoids, etc. have several diseases prevention activity. They also have great role stress tolerance of plants and accumulation of many important bioactive compounds in fruits and vegetables. They several preventive activities in human disease such as antimicrobial, antioxidant, anticancer, anti-inflammatory and wound healing capacity. [3]

2. Role of Phytochemicals in Cancer Prevention:

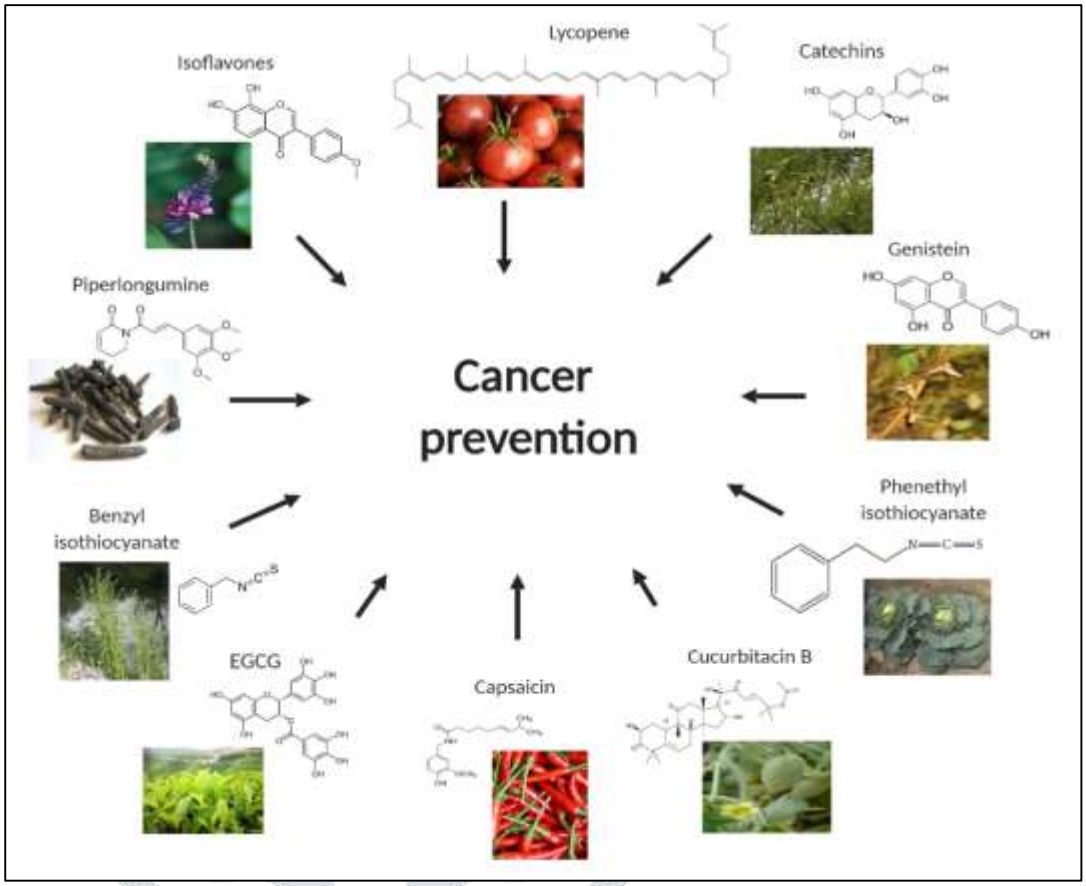

Figure 2: Phytochemicals in Cancer Prevention

The use of synthetic, natural or biological agents to minimize the occurrence of cancer in healthy individuals is defined as cancer chemoprevention. This complex activation consequently influences the cellular defense mechanism counting phase second detoxifying enzymes, phase third transports, antioxidative stress potential and other stress defense molecules induction which species (ROS), reactive nitrogen species (RNS) and reactive metabolites of carcinogenic species. They also able to cause death of apoptosis cell in preneoplastic or neoplastic cells via different growth suppression methods comprising the organization of cytochrome C (cyt C) / caspases, cell cycle catch, the embarrassment of the nuclear factor - KB (NF-KB), Janus Kinase (JAK) - signal transducer and activator of transcription (Stat) signaling pathways, resulting in the tumor progression reticence. [9]

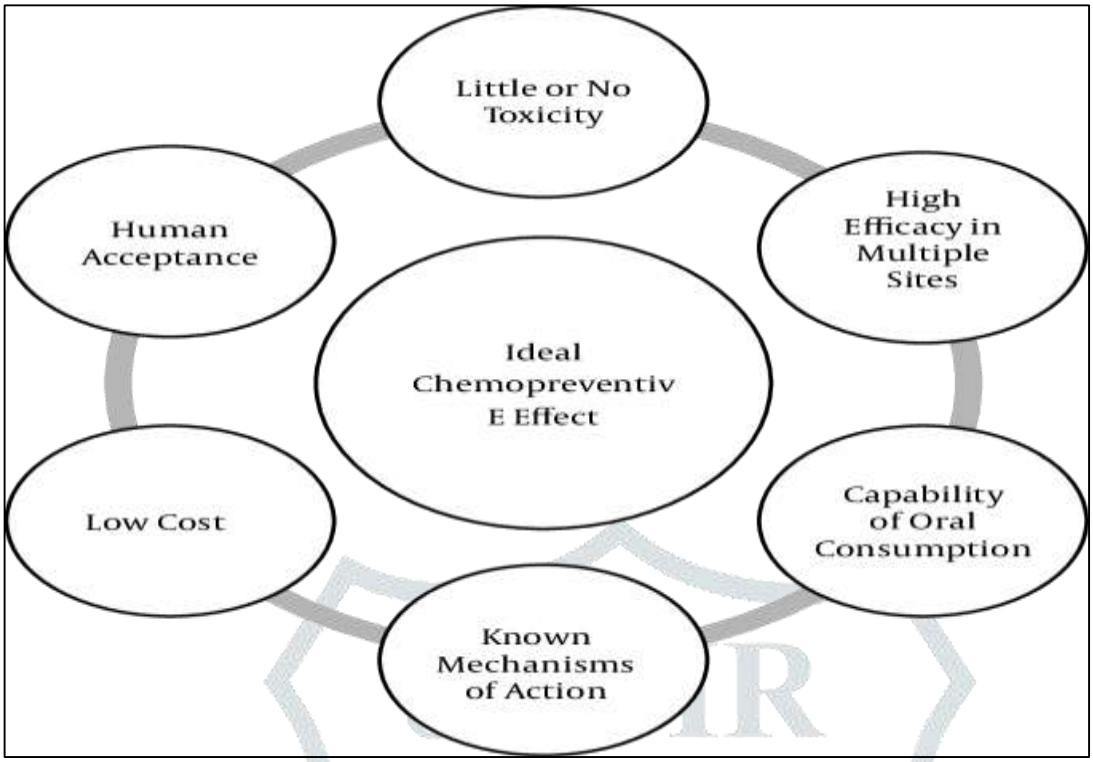

Figure 3 : **The Characteristics of an Ideal Chemo preventive Agents**

3. Role of Phytoconstituents in Prevention of COVID-19:

Phytochemicals or Phytoconstituents are plant metabolite produced by the plants which possess therapeutic effects and beneficial to human in treatment of disease. It is also available as a nutraceutical in which they are found to provide health benefits. The phytochemicals possessing antiviral properties include alkaloids, polyphenol, Polysaccharides, flavonoids, Lecithin's, proteins, Terpenes, lignans, coumarins, saponins, quinones, proanthocyanidins, steroids, thiosulfates, etc. The mechanism of action of some includes alkaloids which act by blocking the binding of virus, inhibit virus growth and reduce virus titres in lungs. Most plants possessing antiviral property have phytochemicals which have the ability to inhibit different steps of virus attack and replication, even though the data regarding the mechanism of action of particular phytochemical is unavailable. [11]

Table 3 : **Role of Phytochemicals in COVID-19 and its Mechanism of Action.**

Phytochemicals	Mechanism of action	Corona virus types
Flavonoids: Luteolin, apigenin, quercetin, Kaempferol, myricetrin	Interfere with the activation of NRP3 inflammasome	SARS beta corona virus
Emodine, anthraquinone	Act by inhibiting the interaction of SARS-Co V S protein with it's receptor	SARS CoV

	ACE2 in dose dependent manner	
Resceratrol, stilbenoid, a natural polyphenol found in red vine grapes, skin of Rachis hypogeal	Inhibit cellular apoptosis after virus attack	MERS CoV

Various Phytoconstituents That are Being Studied for the Treatment of COVID-19 fall Under the Following Classification:

1. **Flavonoids**: Flavonoids are the phenolic compounds present in plants which shows different biological function. Different virtual screening studies carried against Mpro enzyme have proposed several flavonoids like azithromycin, mangiferin, procyanidin-β-2,7-dimethox-yflavaN-4′-O-β-D-glucopyranoside, amentoflavone, hidrosmin, diosmin, gallocathechin gallate, elsamitrucin, pectolinaren, quercetin and iso-quercetin having high binding affinities and thus could be used to combat the current situation. [12]
2. **Alkaloids**: Alkaloids were found to have key roles in inhibition of viral replication as it blocks the function of viral DNA copolymerase. Some alkaloids which are having DNA intercalating activity are sanguinarine, quinine cincho nine, hartmine, chelidonine, coptisine, berberine, palmatin, tetradine, etc and would be used for development of drug molecules. [12]
3. **Glycosides**: Antiviral effects of glycosides have been observed in various studies like the cardiac glycosides were seen effective against both DNA and RNA various including cyto megalo virus, herpes simplex virus, influenza virus and Corona virus. [12]
4. **Anthraquinones**: Anthraquinones derivatives such as hypericin are effective against various other viruses like herpes simplex virus, vaccinia virus and parainfluenza virus. [12]

Various Examples of Phytoconstituents:

1. **Turmeric (Curcuma Longa)**:

- **Introduction** - Curcuma longa is a member of Ginger family (zingiberaceae) and used widely by traditional medical practitioners for the treatment of various ailments. Curcumin is responsible for yellow color. According to World Health Organization (WHO) about 80% of individuals medicine as a source of potential and powerful drug that are derived from medicinal plants. Haldi have traditionally known in India whose rhizomes are along, ovate, pyriform and short branched. Current research on curcumin shows that it's potentially and have anti-inflammatory and anticancer activity. Yellow powder known as curcumin extracted from rhizomes is used as medicinally. Turmeric act as anticancer, antidiabetic, antioxidant, hypolipidemic, antivenom, hepatoprotective, nephroprotective, anticoagulant and possess anti-HIV activity to combat AIDS. [13]

- **Source** - Turmeric plants. [13]

Figure 6 : **Turmeric (Curcuma Longa)**

- **Taxonomical classification**-

  kingdom - Plantae

  Sub kingdom - Tracheobionta

  Super division - spermatophyta

  Division - Magnoliophytes

  Sub class - Zingiberaceae

  Genus- Curcuma

  Species - Longa

  Scientific name- Curcuma longa. [13]

- **Phytoconstituents present in Turmeric**: Curcumin (3-4%), Curcumenol, Curcumene, Eugenol, Beta-carotene, Proteins (6-3%), Fat (5.1%), Minerals (3.5%), Carbohydrates (69.4%) and Moisture (13.1%), Phenolic diketone. [13]
- **Medicinal uses** [23]

- Turmeric has been used as traditional medicine as a household remedy for various issues including biliary disorders, rheumatism and sinusitis, anorexia, cough, diabetic wound, hepatic disorders.
- Turmeric has different health benefits for different diseases such as depression, type 2 diabetes, viral infection, high cholesterol, alziemer disease, arthritis, cancer, headache, acne.
- It is commonly used in Asian foods.
- It has used to flavor or color powders, mustard, butter and cheese. [23]

Figure 7 : **Medicinal Properties of Turmeric**

2. **Ginger (Zingiber Officinale)** :

- **Introduction** - Ginger (Zingiber Officinale) is a member of the zingiberaceae family. It is used in most of the Asian countries. [14] In ginger more than 200 species in 53 genera. Zingiber Officinale used to cure a variety of different diseases like nausea, vomiting, asthma, cough, palpitations, inflammation, dyspepsia, loss of appetite, constipation, indigestion and pain. This plant reported for hepatoprotective activity. Larvicidal activity, analgesics activity, anti-inflammatory activity and immunomodulatory activities. [13]
- **Source** - Zingiber plant. [13]

Figure 8 : **Rhizome of Zingiber Officinale**

- **Taxonomy of Ginger plant-**

  Kingdom - Plantae

  Division - Magnoliophyta

  Order - Zingiberales

  Family - Zingiberaceae

  Genus - Zingiber

  Species - Z. Officinale [15]

- **Phytoconstituents present in ginger** - essential oils, phenolic compounds, flavonoids, Carbohydrates, proteins, alkaloids, glycosides, saponins, tannins, steroid and terpenoids as the major phytochemicals group. These phytochemicals play an important role in the medicinal property of this plant. [15]

- **Medicinal Properties of Zingiber Officinale**

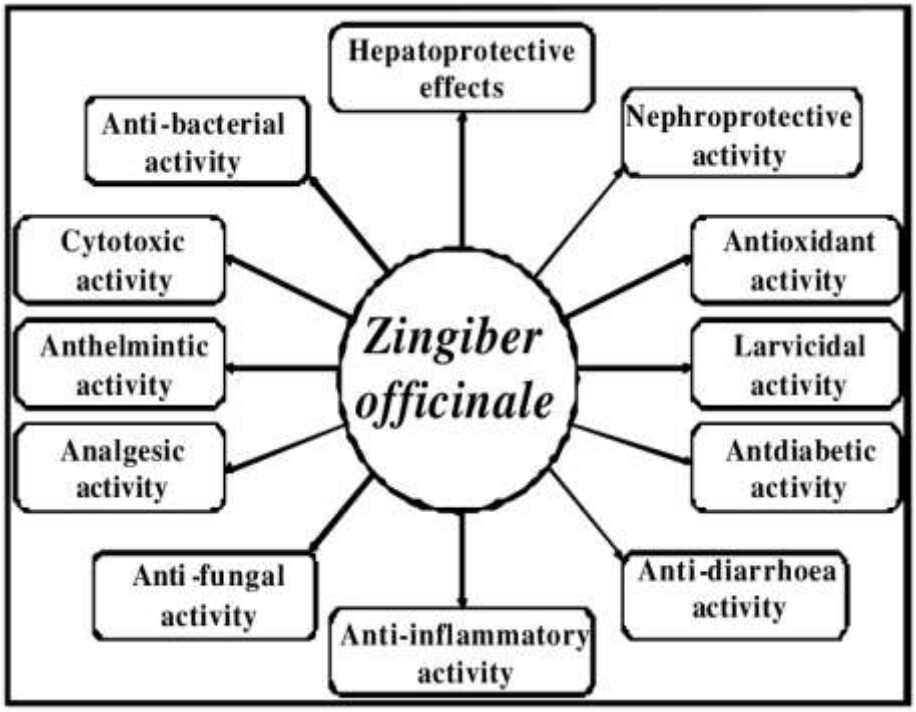

Figure 9 : **Medicinal Properties of Zingiber Officinale**

3. **Cumin (Cumin Cyminum L.)**:

- **Introduction** - Cumin (Cumin Cyminum L.) belongs to the family Apiaceae, also known as umbelliferae family. Cumin is the most popular species of black pepper. Cumin grows to about 30-60cm tall with a glamorous, branched and slender sterm. [17]
- **Source** - Cumin Cyminum plants. [16]

Figure 10: **Cumin Cyminum Plants**.

- **Taxonomical classification** -

  Kingdom - Plantae

  Clade- Angiosperm

  Order - Apiales

  Family - Apiaceae

  Genus - Cuminum

  Species - C. Cyminum. [16]

- **Phytoconstituents present in Cumin** - The various part of the Cumin plant (leaves, shoot, root and flowers) contain similar and different chemical compound. The most important chemical is essential oil. [17]

- **Medicinal Properties of Cumin**

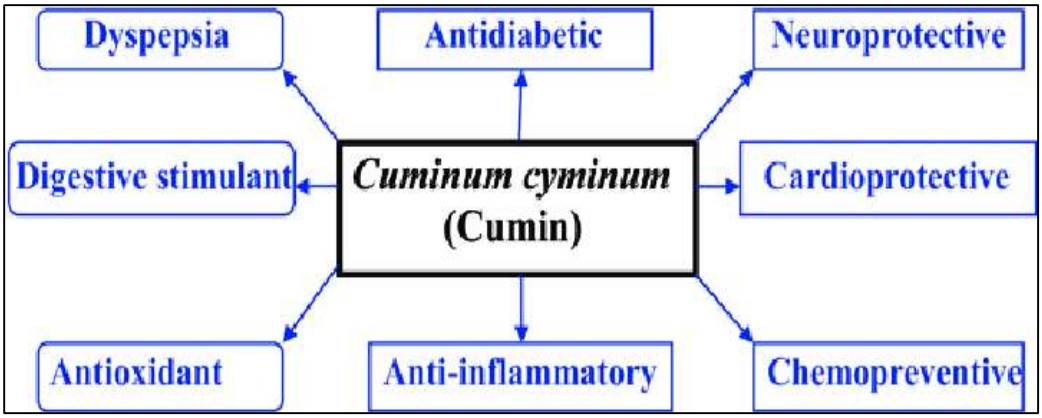

Figure 11: **Multiple Medicinal Properties of Cumin.**

4. **Garlic (Allium Sativum L.)**:

- **Introduction** - Garlic (Allium Sativum L.) belong to family Amaryllidaceae is an aromatic herbaceous annual spice and one of the oldest authenticated and most important herbs that have been used from ancient times as traditional medicine. Allium Sativum is considered as Allium species with onion (Allium Sativum L.) which is used as disease like cold, influenza, snake bite, hypertension. Garlic has been used for purposes of cooking as a spice that can flavor foods during the cooking process. [18]
- **Source** - Allium Sativum perennial plants of amaryllis (Amaryllidaceae) growth for its flavourful bulbs. [18]

Figure 12: Garlic (Allium Sativum)

- **Taxonomical classification** -

  Kingdom - Plantae

  Clade- Angiosperm

  Order - Asparagales

  Family - Alliaceae

  Sub family - Allioideae

  Genus - Allium

Species - Allium Sativum [18]

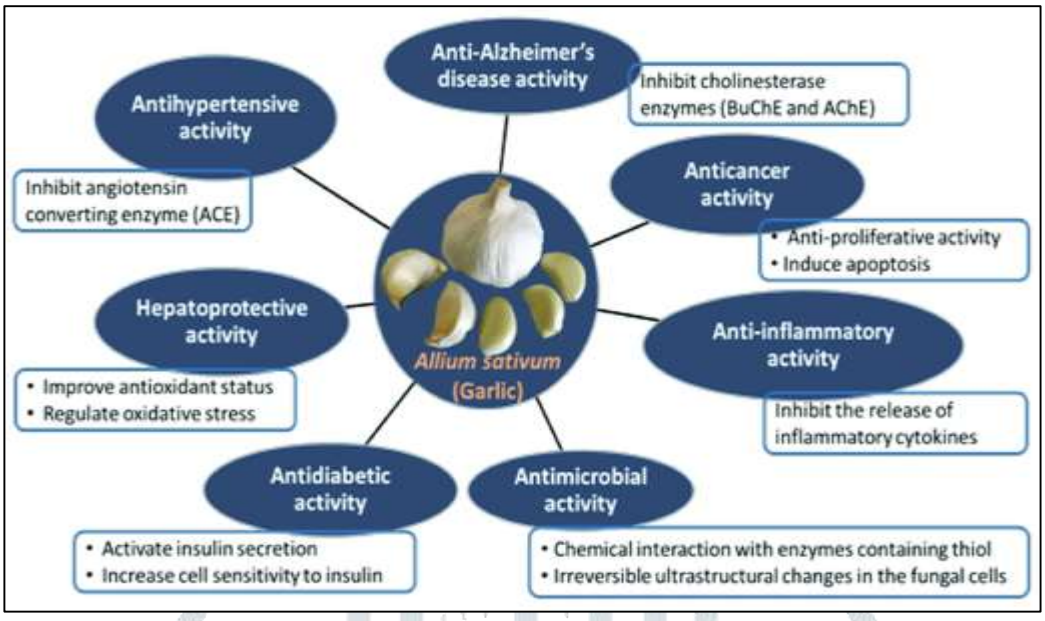

Figure 13 : Pharmacological activity of Garlic.

- **Phytoconstituents present in Garlic** - Carbohydrates (29%), Proteins (albumin) - 56%, Fat muscilage(0.1%), Volatile oils (0.06 to 0.1%). Volatile oil contains Allyl property disulphide, diallyl-disulphate, Allin, Allicin. [18]
- **Medicinal uses**- Disinfectant, Anthelmintic, Antibacterial, useful in high BP and Atherosclerosis, also having cholesterol suppressing property. [18]

5. **Black Pepper (Piper Nigrum):**

- **Introduction** - Black pepper, the king of species (Piper Nigrum L.) is a widely used spice. It has pungent odour. Piper nigrum belongs to family Piperaceae. As of Vietnam is the world's largest procedure, as well as exporter, of pepper, producing 34% of global P. Nigrum crop. Due to its strong pungency, it is regarded as the `king of species ' and it has valuable medicinal potency. Piper Nigrum (Black pepper) exhibit many pharmacological actions like anti platelet, antihypertensive, antispasmodic, antiprotozoal, bioavailability enhancer, memory enhancer, anti-mutagenic, insecticidal, immunomodulator, anti-thyroid, anti-asthmatic, anxiolytic activities, etc. [19]
- **Source** - Black pepper seeds (L.) and pepper fruits. [19]

Figure 14 : **Black Pepper Seeds**

- **Taxonomical classification of Piper nigrum -**

  Kingdom - Plantae

  Sub kingdom - Tracheobionta

  Super division - spermatophyta

  Division - Magnoliophyta

  Class- Magnoliopsida

  Sub class - Magnoliidae

  Order - Piperales

  Family - Piperaceae

  Genus - Piper

  Species - Nigrum L. [19]

- **Phytoconstituents present in Black pepper** - Piperine, sarmentosine, piperamide, peperamine, trichosta, sarmentine, chavicine. [19]
- **Uses of Black pepper** - antiseptic, antispasmodic, anti-inflammatory, diabetes, diuretic, CNS stimulant, blood purifier, Antibacterial, cancer, cough, as carminative, insecticides, etc. [19]

Figure 15 : **Medicinal Properties of Black Pepper**

Conclusion:

From the above-mentioned literature, we concluded that there is various Roles of phytochemicals in COVID-19, cancer prevention, disease prevention and in Neuroprotective. The review conducted showed that the possibility of many phytochemicals might be useful as lead compounds for developing drugs to tackle the COVID-19 pendamic. Phytochemical's supplementation can benefit human health through supplying specific Antioxidative compounds which have preventive role in several diseases. To achieve a suitable concentration of the phytoconstituents, contained in the plants, it is necessary to perform several procedures through which active ingredients are extracted with the adequate solvents, selected according to the solubility and stability of the beneficial substances. Different extraction methods allow obtaining products in pharmaceutical forms suitable for oral or external dosage.

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