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Preservatives from Nature: A Review

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ABSTRACT

Natural food preservatives have been used and known to mankind since a very long time. These are used in both raw as well as cooked food to increase the shelf life of food so that aroma, taste and the food itself can be stored for a longer period of time. Also food degradation is prevented by them. Preservatives, whether natural or artificial, work as in three different ways: Antimicrobial, Antioxidants and Act on enzymes. In antimicrobial, the growth of microbes like bacteria and fungi is inhibited. In antioxidants the process of oxidation is either delayed or stopped. And the one that acts on enzymes stops the ripening or aging of food product. Preservation is important part in many industries, such as the cosmetic and pharmaceutical industries, as the shelf life of many cosmetic and pharmaceutical products is important The present review is an extensive compilation of various preservatives obtained from plan, animal and microbial source.

Key Words: Preservatives, Antioxidants, Antimicrobials, Toxicity, Essential oils.

INTRODUCTION

The world is a land of greenery, where numerous trees grow and are cultivated. These trees supply us with ample amount of natural products that can be used in our day-to-day life. One amongst it is preservatives. Preservatives are substances that commonly added to various foodstuffs and pharmaceutical products in order to prolong their shelf life. The addition of preservatives to such products, especially to those that have higher water content, is essential for avoiding alteration and decomposition by microbes during storage.

Before the discovery of preservatives, food was placed in containers such as clay jars to keep them away from air and moisture which slows the spoiling process, food storage can be traced all the way back to all the ancient civilizations (Egyptian, Greek, Roman, Sumerian, Chinese etc.). Drying food was also a popular preserving method as most bacteria require moisture to grow. Foods like fruits, vegetables and meats were often dried for preservation.

The earliest use of chemical preservatives was salt and sugar, which was used often during the middle ages. The salt has a desiccating effect which can draw water out of the food (another method of drying) but also creates a condition hostile to microbes. Pickling foods is another property of salt. The Eastern Civilizations (India, China etc.) also used spices to preserve their foodstuffs.

Canning was developed in the early part of the 19th century, along with pasteurization which developed by Louis Pasteur in 1862, they revolutionized the preservation of food. Essentially, pasteurization is the method in which the food was heated at high temperature for extended period of time to kill almost all of

the micro-organisms, combined with canning this allowed food to be stored for years and years without spoiling.

The term Preservative is defined as natural or synthetic chemical agent that prevents decomposition by microbial growth or any undesirable chemical change in finished products[1]. Preservatives are used in pharmaceutical industry to prevent the growth of bacteria, mold, fungi and other microbes. They are used in the manufacture of pharmaceutical drugs and cosmetics, for their individual antibacterial (destroying and inhibiting the growth of bacteria), antifungal (destroying and inhibiting the growth of fungus) and antioxidant (to prevent oxidation) properties. [2-4]

CLASSIFICATION OF PRESERVATIVES

Preservatives are classified into two main classes: Artificial Preservatives and Natural Preservatives[5]

Artificial Preservatives

These are chemical substances of synthetic origin used to prevent spoilage and contamination of finished product by micro-organisms e.g. Sodium benzoate, propyl gallate, potassium sorbate etc.

Natural Preservatives

These are the chemical substances obtained from natural sources that offer intrinsic ability to protect products against microbial growth. These include essential oil constituents, flavonoids, phenolic compounds, etc. The natural preservatives are further classified into four types:

- ✓ Plant derived products as preservatives
- ✓ Animal derived products as preservatives
- ✓ Certain microbes and/or their metabolites

Based on mode of action, Natural preservatives are also classified into two groups: Antimicrobial preservatives and Antioxidants[6]

Antimicrobial preservatives are included in the preparations to kill or to inhibit the growth of micro-organisms during manufacture or use. Antimicrobial preservatives are further classified into two main sub-classes: Anti-fungal preservatives and Anti-bacterial preservatives. Anti-fungal preservatives include compounds such as benzoic and ascorbic acids and their salts etc. where as Antibacterial preservatives include compounds such as quaternary ammonium salts, alcohols, phenols etc.

Antioxidants are included in the pharmaceutical products to prevent decomposition from oxidation. Antioxidants are classified into three sub-groups. The first one is known as true antioxidants, or anti-oxygen, probably inhibit oxidation by reacting with free radicals blocking the chain reaction. The second one consists of reducing agents; these substances have lower redox potentials than the drug or adjuvant which they are to be protected, and are therefore, more readily oxidized. Reducing agents may act also by reacting with free radicals. The third one consists of antioxidant synergists which usually have little antioxidant effect themselves but probably enhance the action of antioxidants in the first group by reacting with heavy metal ions which catalyze oxidation.

PRESERVATIVES FROM PLANT SOURCE

Herbs have been used as preservatives due to their antimicrobial activity against certain pathogens and antioxidant property. Herbs and spices contain volatile chemicals that are used in the production of preservatives via distillation and enzymatic action. The aromatic constituents present in the plant exists as a precursor that gets decomposed by enzymes during plant tissue damage creating an anti- bacterial aroma[7]. The list of preservatives obtained from Plant sources are given in Table-1 & Table-2 [8-42].

PRESERVATIVES FROM ANIMAL SOURCE

Certain animal secretions or products produced outside or inside their body act as a source of preservation either in their crude form or after being processed to suitable form. These

secretions/products possess protective functions. The list of preservatives obtained from Animal source is given in Table-3 [43-45].

PRESERVATIVES FROM MICROBIAL SOURCE

Microbes are both harmful (Helicobacter pylori) as well as beneficial for human health (Escherichia coli).Micro-organisms produce certain metabolites during their life cycle which are used as preservatives in various food and pharmaceutical preparations. Following are few preservatives obtained microbial source[46-49]:

1. Acidophilin, a low molecular weight nitrogenous compound from Streptococcus diacetylactis and Leuconostoc citrovorum cultures, has potent antimicrobial activity.
2. Bacteriocins are an extremely heterogenous group of substances. The original definition of bacteriocins referred to proteins of the colicin type produced by colicin type produced by Escherichia coli. Diplococcin & Nisin are well-known bacteriocins produced by Lactococcus cremoris & Lactococcus lactis, respectively. Nisin contains a total of 34 amino acids & unusual lanthionines. Since 1969 Nisin has been approved by the FDA as a preservative in processed cheese, cheese spread pasteurized milk & dairy desserts.
3. Natamycin is a tetraene polyene antibiotic derived from Streptomyces natalensis. It possesses in vitro activity against a variety of yeast and filamentous fungi, including Candida, Aspergillus, Cephalosporium, Fusarium and Penicillium. The mechanism of action appears to be through binding of the molecule to the sterol moiety of the fungal cell membrane. The polyenesterol complex alters the permeability of the membrane to produce depletion of essential cellular constituents. Although the activity against fungi is dose-related, Natamycin is predominantly fungicidal. Natamycin is not effective in vitro against gram-positive or gram-negative bacteria.
4. The lactic acid bacteria (LAB) produce an array of antimicrobial substances such as organic acids, diacetyl, acetoin, hydrogen peroxide, reuterin, reutericyclin, antifungal peptides, and bacteriocins.
Reuterin also showed a significant synergistic effect on L. monocytogenes and a slight additive effect on S. aureus after in combination with nisin although the antimicrobial effect of reuterin against Gram-negative pathogens was not enhanced.

TOXICITY

Some modern synthetic preservatives have been shown to cause respiratory or other health problems. Allergenic peptides present in food preservatives may cause hypersensitivity reactions including allergy or rarely anaphylactic shock. Artificial food preservatives are responsible for causing many health problems related to respiratory tract, heart, blood and other. Although if there is a problem of blood pressure or diabetes then the over consumption of salt and sugar should be avoided. But besides this there is no major health related matters associated with the natural food preservatives. Allergic hazards of few natural preservatives are described in Table-4[50-61].

LEGAL ASPECT / REGULATORY ASPECT

According to European regulation, the only permitted preservatives are those that appear in Annex VI Part 1 or 2 of the EEC Cosmetic Directive 76/768/EEC, including the 7th amending Commission Directive 94/32/EC.
Canada has an established “hotlist” permitting preservatives at established use limits and prohibited preservative compounds. While Japan has two lists viz “permitted in all cosmetics” list and “restricted by end use” list. Brazil has a “permitted preservatives” list which establishes maximum use limits and required warnings Mexico uses a restricted or prohibited list. United States regulation, The FDA does not have an approval process for cosmetic preservatives, Instead it has a “negative” list, restricting or prohibiting the use of certain preservatives. The Cosmetic Ingredient Review (CIR) has reviewed many preservatives, typically stating they are safe up to a maximum concentration.

As per EEC Cosmetic Directives:

1. Preservatives are substances which may be added to cosmetic products for the primary purpose of inhibiting the development of micro-organisms in such products.
2. The substances marked with the symbol (+) may also be added to cosmetic products in concentration other than those laid down in this Annex for other specific purposes apparent from the presentation of the products, e.g. as deodorants in soaps or as anti-dandruff agents in shampoos.
3. Other substances used in the formulation of cosmetic products may also have anti-microbial properties and thus help in the preservation of the products, as, for instance, many essential oils and some alcohols. These substances are not included in this Annex.
4. For the purposes of this list
— "Salts" is taken to mean: salts of the cations sodium, potassium, calcium, magnesium, ammonium and ethanolamines; salts of the anions chloride, bromide, sulphate,acetate.
— "Esters" is taken to mean: esters of methyl, ethyl, propyl, isopropyl, butyl, isobutyl,phenyl.
5. All finished products containing formaldehyde or substances in this Annex and which release formaldehyde must be labelled with the warning "contains formaldehyde" where the concentration of formaldehyde in the finished product exceeds 0.05%.

As per US FDA:
The Federal Food, Drug, and Cosmetic Act provide for the use of chemical preservatives in foods if the chemical is:
1. Generally recognized as safe for such use; or if a food additive is covered by food additive regulations prescribing conditions of safe use;
2. Not used in such a way as to conceal damage or inferiority or to make the food appear better or of greater value than it is;
3. Properly declared on the label of the food in which used.
In addition, the preservative should be food grade, perform its intended function, and be used in accord with good manufacturing practices and, where applicable, in accord with existing food additive regulations.
However, there is no legislation for those natural materials, which, when used for their beneficial effect on the skin, may coincidentally have a positive effect on the total preservative requirement of the formulation[62-65].

CONCLUSION:

A preservative is considered necessary to keep food protected but we should be aware whether we do benefit from the system or not. Few people debate that preservatives are necessary to keep but it is the extent of preservatives use that has become a point of debate.
As food patterns and lifestyles change and vary, influenced by more travel and consumption of a great variety of foods, people are demanding attractive looking and tasty food that is cheap, quick to prepare and has a long storage life. And manufacturers are willing to provide that.
Food has today simply become a commodity that has to be consumed to exist. Commercial products are typically loaded with synthetic preservatives to allow them to remain fresh during the long span between the time of manufacture and the time the customer finishes using it. Although the preservatives used do extend the longevity of the products and help keep them free from bacteria, but the preservatives themselves are often unhealthy. Many cause or promote skin related problems and some are even reported to cause cancer. Individuals who are sensitive to these preservatives need to find preservative-free products. There are many natural preservatives. Natural substances that show antimicrobial activity but are not adequate for broad spectrum activity. Most natural substances are not active against the most threatening microbes, pseudomonas. Others, such as essential oils, require very high concentrations to be effective. Some have offensive odors or colors that would be unacceptable in most of the skin care products. Many also become inactivated by manufacturing procedures and other factors. But one of the many advantages in using your own natural preservatives is that you can eliminate or minimize the use of harmful synthetic preservatives.

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TABLES

Table – 1: List of herbs used as preservatives

SOURCE	CHEMICAL CONSTITUENTS	USES
Aframomum melegueta (Family:Zingiberaceae)	6-Paradol and 6-Shogaol	Antimicrobial, active against Mycobacterium chelonei [M. chelonae], M. intracellulare, M. smegmatis and M. xenopi.
Alpinia speciosa (Family: Boraginaceae)	Pentadecanoic acid, terpinen-4-ol, sabinene	Antibacterial, Antifungal, active against Gram-positive bacteria (Bacillus subtilis, Staphylococcus aureus, Sarcina lutea and Mycobacterium phlei) and Gram-negative bacteria (Escherichia coli and Pseudomonas aeruginosa), as well as Candida albicans.
Arnebia tinctoria (Family: Boraginaceae)	Two naphthoquinones, alkannin and isovalerylalkannin,	Antimicrobial, Antibacterial and Antifungal, active against Bacillus subtilis, Staphylococcus aureus, Streptomyces pyogenes and Candida albicans.
Artemisia selengensis and Artemisia stolonifera (Family: Compositae)	Beta-pinene and beta-caryophyllene	Anti Fungal, active against Candida albicans, Rhodotorula rubra and Aspergillus fumigatus
Bixa orellana (Family: Bixaceae)	delta-tocotrienol	Antibacterial and Antifungal, active against Gram-positive bacteria including Bacillus subtilis, Staphylococcus aureus and Streptococcus faecalis, and exhibited slight activity against Escherichia coli, Serratia marcescens, Candida utilis and Aspergillus niger
Buddleja madagascariensis (Family: Scrophulariaceae)	Mimengoside - A	Protozoocidal, Antifungal, active against Candida strains, Trichomonas vaginalis and Leishmania infantum
Capsicum Species (Family : Solanaceae)	Capsaicin and dihydrocapsaicin	Antimicrobial, Antibacterial and Antifungal, active against bacterial species Bacillus cereus, B. subtilis, Clostridium sporogenes, Clostridium tetani,
Chamaecyparis obtuse (Family: Cupressaceae	Thujaplicin	Antibiotic, active against methicillin-resistant Staphylococcus aureus (MRSA) Escherichia coli, Mycobacterium chelonei [M. chelonae], Pseudomonas aeruginosa and Candida albicans.
Cinnamomum zeylanicum (Family: Lauraceae	Cinnamic aldehyde, trans-Cinnamaldehyde and O-methoxycinnamaldehyde	Antibacterial and Antifungal, active against Aspergillus niger, A. fumigatus, A. nidulans, A. flavus, Candida albicans, C. tropicalis
Clausena anisata (Family: Rutaceae)	Sabinene, Germacrene D	Antibacterial and Antifungal, active against Flavobacterium suaveolens, Serratia marcescens, Alcaligenes faecalis. Geotrichum candidum, Aspergillus parasiticu, P. citrinum and Alternaria alternata.
Cryptolepis sanguinolenta (Family: Apocynaceae)	Neocryptolepine,2 dimeric alkaloids named biscryptolepine and cryptoquindoline	Antibacterial and Antifungal, active against Gram +ve and Gram –ve, Epidermophyton floccosum, Trichophyton rubrum and Aspergillus fumigatus
Cuminum cyminum (Family: Apiaceae)	Cuminaldehyde	Antibacterial against Gram-negative bacteria like E.Coli
Curcuma Longa (Family: Zingiberaceae)	Curcumin I , Curcumin II and Curcumin III	Antibacterial and Antifungal, active against Candida albicans, C. krusei and C. parapsilosis
Cyclamen mirabile	Saponins, cyclaminorin,	Antifungal, most potent compounds against Candida species and

(Family: Myrsinaceae)	deglucocyclamin and cyclamin	Cryptococcus neoformans
Desmodium canum (Family: Fabaceae)	Isoflavanones, named desmodianones A, B and C	Antibacterial and Antifungal, active against B.subtilis, S. aureus, M. smegmatis, E. coli, C. albicans and Neurospora crassa.
Eriosema tuberosum (Family: Leguminosae)	Eriosemaones A-D, Flemicin D	Antifungal Cladosporium cucumerinum and C. albicans
Euphorbia tuckeyana (Family: Euphorbiaceae)	24-Methylenecycloartanol and beta-sitosterol	Antibacterial and Antifungal, Active against Gram positive bacteria and C. albicans.
Garcinia kola (Family: Clusiaceae or Guttiferae)	Polyisoprenyl benzophenone (kolanone), hydroxybiflavanonols	Antibacterial and Antifungal active against E. coli, C. albicans, S.Aureus
Glehnia littoralis (Family: Apiaceae)	1,9-Heptadecadiene-4,6-diyne-3,8,11-triol and (10E)1,10-heptadecadiene-4,6-diyne-3,8,9-triol.	Antibacterial and Antifungal, active against P. aeruginosa, E. coli, S. aureus, B. subtilis and C. albicans.
Juniperus species (Family: Cupressaceae)	Alpha-terpineol (88.4%).	Antibacterial and Antifungal, active against P. aeruginosa, E. coli, B. subtilis and C. albicans
Hypericum roeperanum (Family: Hypericaceae)	5-O-methyl-2-deprenylrheediaxanthone, roeperanone	Anti Fungal, active against Cladosporium cucumerinum and C. albicans.
Isopyrum thalictroides (Family: Ranunculaceae)	Tertiary alkaloid and quaternary alkaloid	Antibacterial and Antifungal
Kigelia pinnata (Family: Bignoniaceae)	Naphthoquinones, isopinnatal, lapachol, phenylpropanoids, p-coumaric and ferulic acid	Antibacterial and Antifungal, active against Corynebacterium diphtheria, Pullularia pullularis
Landolphia owrrience (Family: Apocynaceae)	Steroids, saponins, tannins	Antibacterial, Antifungal and Antimicroabial, active against E. coli, B. subtilis and C. albicans
Lychnophora salicifolia (Family: Asteraceae)	Caryophyllene derivatives, lychnopholic acid and acetyl lychnopholic acid,	Antibacterial and Antifungal, active against C. tropicalis and Trichophyton rubrum,E. Coli, S. Aureus
Morinda Lucida (Family: Rubiaceae)	Anthraquinone, alizarin-1-methyl ethes	Antifungal, Antimicrobial, Aspergillus fumigatus and Trichophyton mentagrophytes
Nelumbo nucifera (Family :Anelumbonaceae)	Kaempferol 3-O-glucoside and luteolin 7-O-glucoside	Antibacterial, Anti-inflammatory, Analgesic and Anti Fungal activities
Ocimum gratissimum (Family:Lamiaceae)	Thymol	Antibacterial and Antifungal, active against Salmonella spp., Klebsiella pneumoniae, Proteus vulgaris, A. fumigatus
Parthenium argentatum (Family : Asteraceae) (Compositae)	Guayulins A and B, and argentatines A-D,	Antibacterial, active against Torulopsis glabrata, Hansenulla [Hansenula] sp., K. pneumoniae, and P. aeruginosa.
Rhazya stricta (Family:Apocynaceae)	Strictanol, tetrahydrosecamine, akuammidine and rhazimanine	Anti Bacterial and Anti fungal, active against S.Aureus, E. Coli, C. Albicans

Table-2: List of essential oils used as preservatives

NAME	SOURCE	CHEMICAL CONSTITUENTS	USES
Birch oil	Betula alba (Family:Betulaceae)	Betulin,betulinic acid and phytochemicals (polyphenols, salicylic acid)	Antioxidant, preservative, antibacterial
Cardamom Oil	Elettaria cardomomum (Family:Zingiberaceae)	Methyl eugenol, terpenes	Antioxidant, relieve tooth ache and digestive disorder
Cinnamon Oil	Cinnamomum zeylanicum (Family: Lauraceae)	Eugenol, eugenol acetate and cinnamic acid, cinnamic aldehyde	Antioxidant, antiviral
Clove Oil	Eugenia caryophylla (Family:Myrtaceae)	Eugenol, Iso eugenol, Eugenol acetate	Antioxidant, antiviral, anthelmentic, relieves toothache, hypoglycemic, antiherpes virus
Coriander	Coriandrum sativum (Family:Umbelliferae)	Terpenes, linalool and pinene	Antioxidant, antibacterial, anxiolytic, carminative, digestive aid
Cumin oil	Cuminum cyminum of (Family:Umbelliferae)	Pinene, phellandrene, Limonene	Antioxidant, antispasmodic, carminative, stimulant and tonic
Eucalyptus Oil	Eucalyptus globulus (Family:Myrtaceae)	A-pinene, b-pinene, terpinen-4-ol, aromadendrene, epiglobulol,	Anti oxidant, a cooling and deodorizing effect on the body,
Fennel Oil	Foeniculum vulgare (Family:Umbelliferae)	A-pinene, myrcene, limonene, 1,8-cineole	Antioxidant, antiseptic, antispasmodic, carminative, depurative, diuretic
Lemon oil	Citrus limonum (Family:Rutaceae)	Ascorbic acid (vitamin c), a-terpinene, linalool, b-bisabolene,	Antioxidant, reducing blood pressure
Sage oil	Salvia officinalis (Family: Labiatae)	Chlorgenic acid, flavones, flavonoid glycoside,cineole, thujone	Anti oxidant, anti biotic, anti fungal, anti spasmodic, astringent
Thyme Oil	Thymus vulgaris (Family: Labiatae)	Thymol, a-thujone, a-pinene, linalool	Antioxidant, antiseptic, antifungal
Marjoram Oil	Origanum marjorana (Family: Labiatae)	Sabinene, a-terpinene, linalool, cis-sabinene hydrate, l terpinen-4-ol	Anti oxidant, analgesic, anti-spasmodic, antiseptic, antiviral, bactericidal
Oregano oil	Origanum vulgare (Family: Labiatae)	Phenolic acids and flavonoids	Antioxidant, antiviral, antibacterial

Table-3: List of Preservatives obtained from Animal Source

NAME	SOURCE	USES
Chitosan	By Deacetylation of Chitin present in exoskeleton of Crustaceans(crabs, shrimps) and Cell wall of Fungi	Antimicrobial against Fungi, Algae, Bacteria and also as Natural Biopesticide
Defensin	Cystiene rich cationic compound found in both vertebrates and invertebrates and also in plants	Antimicrobial against Fungi, Algae, enveloped and non-enveloped viruses
Lactoferrin/ Lacto-transferrin	Found in Human Milk, Animal Milk (Cow milk), Saliva, Tears	Antibacterial, Antiviral, Antifungal, Anticancer and Body immunity
Lacto-peroxidase System	A Peroxidase enzyme secreted from mammary, salivary and other mucosal glands	Antibacterial, Antiviral, Antitumour (Breast Cancer), Preservative in Cosmetics
Lysozyme/ Muramidase	Found in Human Milk, Animal Milk (Cow milk), Saliva, Tears, neutrophils and also egg white	Antibacterial (Gram positive bacteria) Immunity Booster
Pleurocidin	Isolated from the mucus membranes of winter flounder (Pseudopleuronectes americanus)	Antibacterial, Antifungal, Antiviral and Antiparasitic
Lard	Purified internal fat obtained from the abdomen of hog Sus scrofa Linn.	Preservative

Table-4: Allergic hazards of few natural preservatives

Preservative	Toxicity
Cinnamon oil	Burning sensation in mouth, chest and stomach, gastrointestinal problems and sleeplessness persisting for 5 hrs.
Capsicum species	Powerful irritant produces erythematic and burning without blistering human skin, produces severe gastritis and diarrhea.
Curcuma Longa	Gastric ulceration due to reduction in the mucin content of gastric juice, fairly nontoxic, side effects generally limited to mild stomach distress.
Cuminum cyminum	Gastrointestinal ulceration or bleeding from stomach
Juniperus species	Irritating to eyes and mucous membranes. Produce hemorrhagic gastritis when ingested. Systemic effects include weakness and central nervous depression, with hypothermia and respiratory failure.
Ocimum gratissimum	Mild local irritant. Resembles phenol in its systemic actions but less toxic, produces gastric pain, nausea, vomiting, central hyperactivity, occasionally convulsions, coma, cardiac & respiratory collapse.

REFERENCES

1. Council for Agricultural Science and Technology, Naturally occurring antimicrobials in food, Task Force Report, Nr 132. Ames, Iowa, Council for Agricultural Science and Technology,1998
2. Parfitt K, "Martindale:The Complete Drug Reference" 32 nd Ed., Pharmaceutical Press, Massachusts ,1999.
3. Boyce MC, Electrophoresis, 2001, 22, 1447-1459.
4. Hang HY, Lai YC., Chromatogr, 2003, 993 , 153-164

5. Singh A, Sharma PK, Garg G, Natural products as preservative, International Journal of Pharma and biosciences,2010, 1(4):601-612
6. Gould G.W., Industry perspective on the use of natural antimicrobials and inhibitors for food applications. J Food Protect Suppl,1996, 59: 82-86
7. Archana A.B., Varsha M.J., Nikam S.R. and Vilasrao J.K., Antibacterial potential of herbal formulation, Res J Microbiol, 4: 164-167
8. Bashir A K, Abdalla A A, Alkaloids with antimicrobial activity from the root of Rhazya stricta Decn. growing in United Arab Emirates, Arab Gulf Journal of Scientific Research, 1994, 12(1): 119-131.
9. Binutu O A, Adesogan K E, Antibacterial and antifungal compounds from *kigelia pinnata"*. Planta medica, 1996, 62(4): 352-353.
10. Calis, I, Satana M E, Triterpene saponins from cyclamen mirabile and their biological activities, Journal of natural products, 1997, 60(3): 315-318.
11. Cimanga K, Bruyne T., Antibacterial and Antifungal activities of Neocryptolepine, Biscryptolepine and Cryptoquindoline, alkaloids isolated from cryptolepis sanguinolenta, Phytomedicine, 1998, 5, 3: 209-214.
12. Delle Monache G, Botta B,Antimicrobial Isoflavanones From Desmodium Canum, Phytochemistry ,1996, 41(2): 537-544.
13. Ebi G.C., Ofoefule, Investigations into the folkloric antimicrobial activities of landolphia owrrience, Phytotherapy research, 1997, 11(2): 149-151.
14. Alfy El, Tanbouly El, Naphthoquinones of arnebia tinctoria (forssk), Egyptian journal of pharmaceutical sciences, 1996, 37(1/6): 65-70.
15. Fernandez M, Lanza D, Biological activities of buddlejasaponin isolated from buddleja madagascariensis and scrophularia scorodonia, Pharmazie, 1997, 52(1): 76-77.
16. Ascenso A, Ferreira, Antimicrobial activity and phytochemical study of euphorbia tuckeyana, Fitoterapia, 1996, 67(1): 85-86.
17. Galal AM, Antimicrobial activity of 6-paradol and related compounds, International journal of Pharmacognosy, 1996, 34(1): 64-69.
18. Chinyanganya F, Gundidza M, Phytoconstituents and antimicrobial activity of the leaf essential oil of clausena anisata (willd.) J.d. hook ex. Benth, Flavour and fragrance journal ,1994, 9(6): 299-303.
19. Anderson Wa, Moo-young M, Antimicrobial activity of annatto (bixa orellana) extract, International journal of Pharmacognosy, 1996, 34(2): 87-90.
20. Koyama, S., Yamaguchi Y., A new substance (yoshixol) with an interesting antibiotic mechanism from wood oil of japanese traditional tree (kiso-hinoki), chamaecyparis obtuse, General Pharmacology ,1997, 28, 5: 797-804.
21. Ffuzzati N, Weiguang Ma, Four chromones from eriosema tuberosum, Phytochemistry 1996, 41(5): 1287-1291.
22. Madubunyi II, Obi SKC, Nwebube, NI, Antihepatotoxic and antimicrobial activities of harungana madagascariensis leaf extracts, International journal of pharmacognosy, 1995, 33(2): 129-134.
23. Madubunyi II, Antimicrobial activities of the constituents of garcinia kola seeds, International journal of pharmacognosy, 1995, 33(3): 232-237.
24. Martinez R, Vazquez M, Antimicrobial properties of argentatine a, isolated from parthenium argentatum, Fitoterapia, 1994, 65(4): 371-372.
25. Matsuura H, Saxena G, Antibacterial and antifungal polyine compounds from Glehnia littoralis ssp. Leiocarpa, Planta medica, 1996, 62(3): 256-259.
26. Filho C, Miguel OG, Antimicrobial activity of constituents isolated from Lychnophora salicifolia (asteraceae)" Phytotherapy research, 1996, 10(8): 694-696.
27. Ndounga M, Ouamba J.M, Antibacterial and antifungal activities of essential oils of Ocimum gratissimum and o. Basilicum from congo, Fitoterapia, 1997, 68(2): 190-191.
28. Aboutabl EA, Pooter HL, Chemical composition and antimicrobial activity of essential oil of leaf, stem and rhizome of alpinia speciosa (j.c. wendl) k. Schum. Grown in egypt" Flavour and fragrance journal, 1995, 10(2): 63-67.
29. Burney S, Landman D, In vitro activity of Cinnamomum zeylanicum against azole resistant and sensitive candida species and a pilot study of cinnamon for oral candidiasis, American journal of chinese medicine ,1996, 24(2): 103-109.
30. Hostettmann K, Rath G, Antifungal anthraquinones from morinda lucida, International journal of pharmacognosy, 1995, 33(2): 107-114.
31. Mavi S, Potterat O, Xanthones from Hypericum roeperanum, Phytochemistry ,1996, 43(2): 513-520.

32. Chandra A, Nair M,Novel bioactivities of curcuma longa constituents, Journal of natural products, 1998, 61, 4, 542-545
33. Kulkarni PR, Shetty RS, Antimicrobial properties of cumin, World journal of microbiology & biotechnology, 1994, 10(2): 232-233.
34. Singh HB, Srivastava M, Cinnamon bark oil, a potent fungitoxicant against fungi causing respiratory tract mycoses, Allergy (copenhagen) ,1995, 50(12): 995-999.
35. Stassi V, Verykokidou E, The antimicrobial activity of the essential oils of four Juniperus species growing wild in greece'' Flavour and fragrance journal , 1996, 11(1): 71-74.
36. Saeed A, Wassel G, Flavonoids of nelumbo nucifera gaertn and biological evaluation, Egyptian journal of pharmaceutical sciences, 1996, 37(1/6): 585-595.
37. Johnson B, Christopher, Substantial uv-b-mediated induction of essential oils in sweet basil (ocimum basilicum), Phytochemistry, 1999, 51 (4): 507–510.
38. Bozin B, Mimica-dukic N, Characterization of the volatile composition of essential oils of some lamiaceae spices and the antimicrobial and antioxidant activities of the entire oils, J. Agric. Food che March 2006, 54 (5): 1822–8.
39. Cheng PW, Chiang LC, Antiviral activities of extracts and selected pure constituents of Ocimum basilicum, Clin. Exp. Pharmacol. Physiol, October 2005, 32 (10): 811–6.
40. Premanathan M, Rajendranathan S, A survey of some Indian medicinal plants for anti-human immunodeficiency virus (hiv) activity, The indian journal of medical research, 2000, 112: 73–7.
41. Benencia F, Courrèges MC, In vitro andin vivo activity of eugenol on human herpesvirus, Phytotherapy research, 2000, 14 (7): 495–500.
42. Chih- Chun, Wen, Specific plant terpenoids and lignoids possess potent antiviral activities against severe acute respiratory syndrome coronavirus, Journal of medicinal chemistry, 2007, 50 (17): 4087–95.
43. Evans W. Saunders WS, Ed. Trease and Evans: Pharmacognosy, 15th Edn, Edinburgh, 2002
44. Yadav A.S. and Singh R.P., Natural preservatives in poultry meat products, Natural Product Radiance,2004, 3 (4): 302-303
45. Kar A, Pharmacognosy and Pharmacobiotechnology,Second edition,New Age International Publishers,New Delhi,2007
46. Forster RK, Jones DB, Fusarium solani keratitis treated with natamycin (pimaricin), 18 consecutive cases." Arch. Ophth, 1972, 88:147.
47. Debevere J, El-Ziney, jakobsen M, Natural Antimicrobial Systems. Reuterin In naidu, (ed), Crc press, London, 2000, 567-587.
48. Maldonado A, Ruiz-barba JL,The locus responsible for production of plantaricins, a class iib bacteriocin produced by Lactobacillus plantarum LPCO10, is widely distributed among wild-type lact Plantarum strains isolated from olive fermentations. International journal of food microbiology, 2002, 77: 117–124.
49. Maldonado A, Ruiz-barba JL, Production of plantaricin nc8 by lactobacillus plantarum nc8 is induced in the presence of different types of gram-positive bacteria, Archives of microbiology, 2004, 181:8–1.
50. Millard L G, Contact sensitivity to toothpaste, Br Med J, 1973, 1(5854):a676- 676.
51. O'Neil M.J. (Ed.). "The Merck Index - An Encyclopedia Of Chemicals, Drugs, And Biologicals", 13th Edition, Whitehouse Station, NJ, Merck And Co., Inc., 2001., P. 296.
52. Lewis R.J. Sr. (Ed) Sax's Dangerous Properties of Industrial Materials". 11th Edition. Wiley-Interscience, Wiley &Amp; Sons, Inc. Hoboken, NJ. 2004, 690.
53. Gupta B, Kulshrestha VK, Srivastava RK, Mechanisms of curcumin induced gastric ulcer in rats. Indian J Med Res. 1980;71:806-814
54. Ammon H P T, Wahl M A. Pharmacology of Curcuma Longa, Planta Med, 1991, 57:1-7.
55. Sreejayan N, Rao MNA, Free Radical Scavenging Activity of Curcuminoids. Arzneimittelforschung. 1996, 46: 169-171.
56. Deodhar Sd, Sethi R, Preliminary Study on Antirheumatic Activity Of Curcumin (Diferuloyl Methane), Indian J Med Res. 1980, 71: 632-634.
57. Srimal RC, Dhawan BN. "Pharmacology of Diferuloyl Methane (Curcumin), A Non-Steroidal Anti-Inflammatory Agent". J Pharm Pharmacol.1973, 25:447-452.
58. Gupta B, Kulshrestha Vk, Srivastava Rk, Mechanisms of Curcumin Induced Gastric Ulcer In Rats, Indian J Med Res. 1980, 71:806-814.
59. Jenner PM,Food and Cosmetics Toxicology, 1964, 2: 327-343.
60. Gosselin R.E., H.C. Hodge, Clinical Toxicology of Commercial Products. 4th Ed. Baltimore", Williams and Wilkins, 1976. P. Ii-170.

61. Gosselin R.E., H.C. Hodge, Clinical Toxicology of Commercial Products. 5th Ed. Baltimore, Williams and Wilkins, 1984:189.
62. http://Pubchem.Ncbi.Nlm.Nih.Gov/Summary/Summary.
63. http://Www.Tccscc.Org/Documents/Scc-Tc%20presentation%20final%202-15-2011.Pdf. http://www.Fda.Gov/Iceci/Compliancemanuals/Compliancepolicyguidancemanual/Ucm074583.Htm
64. http://www.Leffingwell.Com
65. http://Www.Dweckdata.Com

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