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Phenol-An effective antibacterial Agent

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ABSTRACT

Phenol displays effective antimicrobial activity in-vitro against a wide range of organisms such as bacteria (both gram positive and gram negative), yeasts and molds [1-5]. Phenols combine with nuclear receptors involved in growth and adipogenesis maintainance. Few reports have explored their effects on growth in humans. Phenolic substituents are employed in variety of daily products such as cosmetics(parabens), antibacterial soaps(triclosan) and polycarbonate plastics or epoxy resins used in can linings [6-10]. Phenolic compounds are used as antibacterials which include pure form of phenol and by products with halogenos and alkyl groups. They act by denaturing and coagulating proteins.

INTRODUCTION

Phenol (carbolic acid) is one amongst the oldest antibacterial agents. It acts as a bacteriostat by inhibiting biological process of bacteria at concentrations of 0.1%-1% and is fungicidal in action at concentration of 1%-2%. 5% concentration kills anthrax spores in 48 hours. The antiseptic activity is increased by EDTA and heat temperatures; it's decreased by alkaline medium (through ionization), lipids, soaps, and cool temperatures[11-20]. Concentrations >0.5% exert an localised anesthetic result, whereas 5% solution is powerfully allergic and burns to tissues. Oral consumption or in mixing up with skin will cause general toxicity, mainly affecting systema nervosum centrale and vessel effects; and might result in death [21-25]. Phenol has sensible penetration power into organic content and is principally used for medical aid of apparatus or organic content that square measure to be eliminated (eg, infected food and excreta). Owing to its irritant action and caustic properties and capable general toxicity, it's not used very much like an antibacterial presently, except to treat infected areas, eg, the infectious omphalos of neonates. It is additionally incorporated into cutaneal applications for itching, stings, bites, burns, etc, owing to its anesthetic action and antibacterial activity to alleviate itching and helps to manage infections [26-30].

NATURAL SOURCES OF PHENOLS

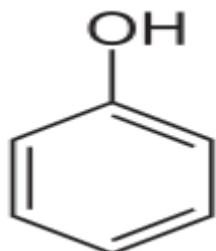
Phenols are derived commonly in nature; examples embrace aminoalkanoic acid, one in all the quality amino blocks found in many proteins; vasoconstrictive (such as adrenaline), a stimulant endocrine originating from adrenal medulla; monoamine neurotransmitter [31-35], a neurochemical within the brain; and urushiol, associate pain secreted by poison Hedera helix to forestall animals from uptake its leaves. Several of the additional advanced type of phenols used as flavouring agents and aromas square measure extracted from essential oils coming from plants. Parenthetically, vanillin, the principal flavoring in vanilla, is obtained from vanilla beans, and sweet-birch oil, that includes a unusual minty taste and odour, is extracted from wintergreen. Different types of phenols obtained from plants embrace phenol [36-40], isolated from thyme, and eugenol is obtained from cloves **Figure 1**.



Figure 1: Poison ivy (*Toxicodendron radicans*) is a natural source of the phenol ...
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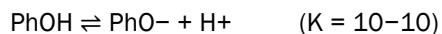
CHEMISTRY OF PHENOL

- 1) **IUPAC Name:** Phenol
- 2) **Other names:** Benzenol, Carabolic acid, Phenyllic acid, Hydroxybenzene, Phenic acid
- 3) **Chemical Formula:** C₆H₆O
- 4) **Molecular mass:** 94.11 g•mol⁻¹
- 5) **Appearance:** Transparent crystalline solid
- 6) **Odor:** Sweet and tarry
- 7) **Melting Point:** 40.5 °C (104.9 °F; 313.6 K)
- 8) **Boiling Point:** 181.7 °C (359.1 °F; 454.8 K)
- 9) **Structure:**



- 10) **Solubility:** Soluble in water and the Na⁺salt form of phenol is more soluble in phenol

Phenol is weakly acidic and at high pHs gives the phenolate anion C₆H₅O⁻ (also called phenoxide) [41-45]:



Compared to aliphatic alcohols, phenol is about 1 million times more acidic, although it is still considered a weak acid. It reacts completely with aqueous NaOH to lose H⁺ [46-50], whereas most alcohols react only partially **Figure 2**.



Figure 2: Solid form of phenol

PHENOL COMPOUNDS

- a) **Cresol (cresylic acid)** could be a mixture of ortho-, meta-, and paracresols and their isomers. It is a colorless liquid; but, exposure to light and air, it turns pink, then chromatic, and at last dark brown. A two hundredth resolution of either pure or saponated phenol “lysol” in plignt is often used as a disinfectant for inanimate objects [51-55].
- b) **Hexachlorophene (a trichlorinated bis-phenol)** incorporates a robust organic process action against several gram-positive organisms (including staphylococci) however solely some gram-negative ones. It is used widely in medicated soaps. Frequent washings on a daily basis with antibacterial soaps result in adequate retention of residue on the skin to supply prolonged organic process action. The laundry with alternative soaps promptly removes these residues [56-58]. Continuous exposure of skin to high concentrations of antibacterial might result in adequate absorption of the antiseptic to cause spongiform degeneration of the substantia alba within the brain, cerebral dropsy, and nervous disorders. To stop such neurotoxicity, merchandise containing >0.75% antibacterial are given on prescription. Accidental oral intake of antibacterial ends up in acute poisoning [59,60].
- c) **Pine tar** is a viscid blackish brown liquid, used primarily for antiseptic bandaging of wounds of the hoof and horn. Pine tar contains phenol derivatives that provide antimicrobial properties.
- d) **Chloroxylenols** square measure broad-spectrum bactericides with a lot of activity against gram-positive than gram-negative bacterium. They are active in basic pH [61-64]; but when in contact with organic matter diminishes their activity. Streptococci show a lot of vulnerability than staphylococci to these agents.
- e) **Parachlorometaxylenol (PCMX) and dichlorometaxylenol (DCMX)** area the two most ordinarily used members of this cluster. DCMX is a lot of active than PCMX. Robust solutions of those compounds will cause irritation and have a disagreeable odor [65-70]. A 5% of chloroxylenol (eg, PCMX) (in α -terpineol, soap, alcohol, and water) is diluted with water (1:4) for skin sterilization and (1:25 to 1:50) for wound cleansing and irrigation of the womb and duct. PCMX is additionally combined with bactericide to boost its antibacterial drug spectrum and to forestall contamination by gram-negative organisms.

Exposure to phenol could occur from the utilization of some medicative product (including throat lozenges and ointments). Phenol is extremely irritating to the skin, eyes, and secretion membranes in humans when acute (short-term) inhalation or dermal exposures. Phenol is taken into account to be quite venomous to humans via oral exposure [71,72,73]. Anorexia, progressive weight loss, diarrhea, vertigo, salivation, a dark coloration of the excretion, and blood and liver effects are rumored in inveterately (long-term) exposed humans. Animal studies have rumored reduced craniate body weights, growth retardation, and abnormal development within the offspring of animals exposed to phenol by the oral route. EPA has classified phenol as a bunch D, not distinctive on human carcinogenicity [74].

Mechanism of action

Phenol will act on microorganisms in 2 totally different ways: growth inhibition (bacteriostasis, fungistasis) or fatal action (bactericidal, agent or viricidal effects). Only the fatal effects are of interest in medical aid and, because the objects of treatment have no inherent means that of defence, deadliness is that the desired objective [75,76,77]. Although microbiologists are operating for more than a century on the problems related to medical aid, understanding of the mode of action of active molecules remains vague: varied hypotheses exist however few certainties. Several authors have long maintained that phenols act in a non-specific manner, in contrast to antibiotics that have distinct cellular targets inside the organism. Although several studies still ought to be performed during this field, it's clear that this distinction can't be created for a few molecules [78-80]. Phenols are sometimes complicated formulations of active molecules, sometimes additionally containing co-solvents, chelating agents, acidic or alkaline agents, or surface-active or anti-corrosive products. In an analysis of the action of a phenol, it may often be difficult to distinguish between the primary stage (characteristic of the mode of action) and the secondary stage (merely a consequence of the action).

1) Action on the external membrane of the bacterial wall

A bacteria is protected against its surroundings by a membrane, the integrity of that is essential for survival of the bacteria. This membrane consists of basic compounds such as phospholipids and lipopolysaccharides, and is made stable by Mg⁺⁺ and Ca⁺⁺cations. Thus, if ionizing disinfecting molecules are absorbed or repelled by electrical charges at the initial contact and absorption stage, the subsequent means that of action can theoretically be possible [81-83]:

- non-polar molecules could dissolve and enter the supermolecule part
- specific carrying systems can lead different molecules through the membrane
- different molecules are going to be ready to disturb the organisation of the membrane by remaining certain to bound sites.

2. Action on the bacterial wall

The bacterial wall is important, as this provides rigidity and differs considerably between Gram-positive and Gram-negative bacteria. This diversity leads to great variation in the response of the hydrophilic antibacterials.

3. Action on the cytoplasmic membrane

An active molecule of phenol, may penetrate the cytoplasmic membrane in the following ways [84,85]:
a) passive diffusion which is non-specific and slow
b) active transport which is specific, enabling the accumulation of products in bacteria after either transformation or binding to a membrane protein.

4. Action on the cytoplasm and nucleus

The phenol mechanism may operate on the cytoplasm and nucleus at the chromosome level.

5. Action on bacterial spores

The solidity and also the presence of dipicolinic acid in microorganism spores build these forms far more tough against antibacterials than vegetative forms [86,87]. The active disinfectant phenols embrace extremely oxidising merchandise, akin to oxide and gas, which can destabilise this structure in spores.

USES OF PHENOL

- Approximately two-third of the entire phenol made worldwide is employed to arrange reagents utilized in plastic producing industries. Most of the items around us are either made of plastics or have plastic parts in them. The condensation reaction of phenol with ketone produces bisphenol that is extensively utilized in chemical compound industries to synthesis numerous epoxide resins and polycarbonates [88,89].
- The chemical action reaction of phenol with aldehyde is employed to commercially prepare phenoplast resins. The ensuing organic compound is thought as phenol-formaldehyde organic compound, commercially it's marketed by the name of Bakelite. Bakelite is extensively employed in electrical switches and vehicles thanks to its property of withstanding extreme conditions of warmth and resistance to electricity and alternative chemicals. The intermediate created throughout the chemical action reaction is termed novolac, this can be an organic compound and is employed as a binding agent or adhesive in several industries. Novolac is additionally used for protecting coating functions [90,91,92].
- Phenol is additionally utilized in the study and extraction of bio-molecules. biological science finds application of phenol within the extraction of nucleic acids from tissue samples for more investigations.

- Phenol is also used in cosmetic industry in the manufacturing of sunscreens, skin lightening creams and hair coloring solutions.
- Used to turn out epoxy resins for paints coatings and mouldings, and in polycarbonate plastics, acquainted in CDs and domestic electrical appliances.
- Caprolactam is employed within the manufacture of nylon and polymer plastics for a good vary of product, together with carpets, clothing, fishing nets, moulded elements and packaging [93,94].
- Intermediate of phenol is employed as associate inhibitor in rubber manufacture, associated as an intermediate in herbicides, dyes and pigments, and pharmaceuticalsIt is employed to form isocyanates for the assembly of polyurethanes, with a good vary of uses from paints and adhesives to enlarged foam cushions.
- These compounds are employed in the manufacture of surfactants, detergents and emulsifiers, and additionally in insect powder and plastics production.
- Used in medical antiseptics and bactericides admire transmission control protocol and Dettol. Additionally employed in fungicides for timber preservation and as additives to inhibit microorganism growth in several products; accustomed manufacture a variety of pesticides.
- This is employed in the assembly of analgesic and alternative prescription drugs [95-99].

CONCLUSION

In conclusion, there's associate imperative have to be compelled to investigate a lot of the character of the repressive and fatal effects of phenols as antibacterial agents on a variety of microorganisms and microbic entities. The doable multiple target sites and concentration-dependent effects would type a crucial side of such studies, which might additionally give an improved understanding of intrinsic properties and show microorganism resistance mechanisms and of the doable linkage between biocide usage and antibiotic resistance.

Although the notion of a target within the microorganism cell is usually elicited within the case of phenols, this side remains rather obscure with respect to antibacterial. Nor can antibacterial action be thought-about specific to a selected microorganism species, whereas such specificity is common in antibiotics. However, this clearly masks an explicit disparity involving variations in activity between gram-positive and gram-negative bacteria. One should conjointly bear in mind the principal parameters that condition the action and therefore the effectualness of phenols (e.g. temperature, pH, concentration, time of contact).

The potential conjugated result of many antibacterials conjointly deserves reflection. Again,as the modes of action don't seem to be invariably well outlined, it's troublesome to talk of a synergistic effect. At most, an additive result is exerted once the concentrations of the active ingredients square measure fittingly custom-made. Due to the comparatively scant information of modes of action, and therefore the existence of complicated formulations, product from two completely different manufacturers mustn't be mixed, seeable of the potential antagonistic effects of different product. Brief mention should be created here of microbic resistance to antibacterials, which has no parallel with resistance to antibiotics. Makers at the agricultural and food industries usually claim that the microorganism on their premises became immune to the product used as antibacterial. Very little is thought of the microbic ecology of productionunits in these industries, as analysis during this field isn't systematized. Nonetheless, various studies have shown that bound microorganism become immune to element following chlorination treatment of water.

Future analysis ought to focus on discerning the mode of action of antibacterials on viable microorganism, microorganism beneath stress and microorganism components of a biofilm, beneath the conventional conditions of use.Under such conditions it'll clearly be troublesome to get a 99% reduction in the microorganism gift, pro re nata by the standards of the Association française Delaware normalisation (French Standardisation Association). Cleaning and medical aid should be absolutely effective, limiting contamination to an acceptable minimum level that is compatible with any manufacture.

In recent years, rotation of phenols as disinfectants in hospitals e.g. within the pharmaceutical and food industries, has been advocated to stop the event of microorganism resistance. It has been claimed that, ideally, one disinfectant ought to get replaced by another having a dissimilar mechanism of action.

REFERENCES

1. Singh J et al. Phenolic Content and Antioxidant Capacity of Selected Cucurbit Fruits Extracted with Different Solvents. *J Nutr Food Sci* 2016; 6:565.
2. Shihai Y et al. Solvent Effect on Hydrogen-Bonded Acetic Acid Arginine/Imidazole/Phenol Dyads. *Med Chem Los Angeles* 2016 ;6:604-610.
3. Prakasha A and Umesha S . Biochemical and Molecular Variations of Guaiacol Peroxidase and Total Phenols in Bacterial Wilt Pathogenesis of *Solanum melongena*. *Biochem Anal Biochem*2016; 5:292.
4. Wieners M,et al. The Rare Polypore *Antrodiella citrinella* and Its Special Phenology in the Black Forest National Park Germany. *J Biodivers Endanger Species* 2016;4:168.
5. Fombang EN and Saa WR Production of a Functional Tea from *Moringa oleifera* LAM Leaf Powder: Optimization of Phenolic Extraction Using Response Surface Methodology. *J Nutr Food Sci* 2016 ;6:556.
6. Huber K et al. Phenolic Acid, Flavonoids and Antioxidant Activity of Common Brown Beans *Phaseolus vulgaris* L. Before and After Cooking. *J Nutr Food Sci* 2016 ;6:551.
7. Mir S et al.Treatment of Steroid and Cyclophosphamide-Resistant Nephrotic Syndrome with Mycophenolate Mofetil and High Dose Dexamethasone DEX. *J Nephrol Ther* 2016;6:257.
8. Bagchi A. Protective Effect of Epigallocatechin-3-Gallate EGCG the Major Tea Polyphenolic, Against Intracerebroventricularly Colchicine Induced Oxidative Damage Production in Brain and Cognitive Dysfunction in Mice. *J Alzheimers Dis Parkinsonism* 2016;6:250.
9. Díaz Rivas JO, et al. Gastroprotective Activities of *Buddleja scordioides*-Role of Polyphenols against Inflammation. *J Chem Biol Ther* 2016;2:109.
10. Wyatt BS et al. Sex- and Strain-dependent Effects of Bisphenol: A Consumption in Juvenile Mice. *J Diabetes Metab* 2016;7:694.
11. Rathore AS et al. Determination of Major Polyphenolic Components in *Euphoria longana* Lam. by Validated High Performance Thin-Layer Chromatography Method and Direct Analysis in Real Time Mass Spectrometry. *J Chromatogr Sep Tech* 2016;7:330.
12. Sadegh Hassania S et al. Comparable Study of 4-chlorophenol Removal from Petrochemical Wastewater Using Mesoporous and Microporous Carbons: Equilibrium and Kinetics Investigations. *J Pet Environ Biotechnol* 2016;7:289.
13. Liu H et al. Anti-diabetes and Anti-inflammatory Activities of Phenolic Glycosides from *Liparis odorata*. *Med chem Los Angeles* 2016 ;6:500-505.
14. Jarosławska J et al. Polyphenol-rich Blackcurrant Pomace Counteracts Impaired Antioxidant Status and Serum Lipid Profile in Rabbits Fed a Diet High in Unsaturated Fat. *J Nutr Food Sci* 2016;6:531.
15. Manna E and Maiti S Cardio-Protecting Effect of Natural Bioactive Compound Polyphenol by Inhibiting LDL Oxidation with the Scavenging of Reactive Oxygen Species ROS. *J Clin Exp Cardiol* 2016;7:453.
16. Kawahara Y. Electrospinning of Direct Carbonizable Phenolic Resin-based Nanofibers. *J Textile Sci Eng* 2016;6:257.
17. Shanthi S and Yenkie MKN. P-Nitrophenol: A Model Compound for the Study of Role of PH in the Reaction of Ozone with Phenols. *J Pollut Eff Cont* 2016;4:168.
18. Shobana Devi R and Nazni P. Sensory Characteristics, Total Polyphenol Content and In vitro Antioxidant Activity of Value Added Processed Barnyard Millet Flour Chapattis. *J Food Process Technol* 2016;7:595.
19. Ahmed M et al.Colour Intensity, Polyphenol Content and Antibacterial Capacity of Unheated and Heat-Treated Sahara Honey. *J Food Process Technol* 2016 ;7: 589.
20. Maallah R et al.Electro-Oxidation and Detection of Phenol on Metals Modified Carbon Paste Electrodes. *Toxicol open access* 2016;2:111.
21. Conte R et al. Polyphenols Nanoencapsulation for Therapeutic Applications. *J Biomol Res Ther* 2016;5:139.

22. Shashkov MV and Sidelnikov VN. Separation of Phenol-Containing Pyrolysis Products Using Comprehensive Two-Dimensional Chromatography with Columns Based on Pyridinium Ionic Liquids. *J Anal Bioanal Tech* 2016;7:313.
23. Shaimaa GA et al. Effect of Heat Treatment on Phenolic and Flavonoid Compounds and Antioxidant Activities of Some Egyptian Sweet and Chilli Pepper. *Nat Prod Chem Res* 2016;4: 218.
24. Dua B et al. Expansion of T regulatory cells in lepromatous leprosy is mediated by Phenolic glycolipid-1. *J Med Microbiol Diagn* 2016;5:226.
25. Aroyeun SO and Jayeola CO. Effects of Green Tea Extracts on the Caffeine, Tannin, Total Polyphenolic Contents and Organoleptic Properties of Milk Chocolate. *J Food Process Technol* 2016;7:579.
26. Maleš Ž and Bojic M. Antioxidant Potential of Polyphenols: In Need for Critical Assessment of In Vitro Results. *J Pharmacogn Nat Prod* 2016;2:e104.
27. Bouyahya A et al. Determination of Phenol Content and Antibacterial Activity of Five Medicinal Plants Ethanolic Extracts from North-West of Morocco. *J Plant Pathol Microbiol* 2016;7:342.
28. Rosa LS et al. Anticancer Properties of Phenolic Acids in Colon Cancer – A Review. *J Nutr Food Sci* 2016;6:468.
29. Khan A. Maize *Zea mays L.* Genotypes Differ in Phenology, Seed Weight and Quality Protein and Oil Contents when Applied with Variable Rates and Source of Nitrogen. *J Plant Biochem Physiol* 2016;4:164.
30. Elsadig Karar MG et al. Phenolic Profile and *In Vitro* Assessment of Cytotoxicity and Antibacterial Activity of *Ziziphus spina-christi* Leaf Extracts. *Med chem Los Angeles* 2016;6:143-156.
31. Alsuhabani A et al. Ultrasound Guided Phenol Block of the Obturator Nerve for Severe Adductor Spasticity: A Pilot Study. *Int J Neurorehabilitation* 2016;3:1000202.
32. Rajput JD et al. Design, Synthesis and Biological Evaluation of Novel Class Diindolyl Methanes DIMs Derived from Naturally Occurring Phenolic Monoterpenoids. *Med chem Los Angeles* 2016;6:123-128.
33. Song M et al. Investigation on the Profile of Phenolic Acids and Flavonoids with Antioxidant Capacity in Florida Highbush *Vaccinium corymbosum L.* and Rabbiteye *Vaccinium virgatum* Blueberries. *J Exp Food Chem* 2016;2:105.
34. Zahra HK et al. Critical Behavior of the Electrical Conductivity for the Binary Mixture of Water and Phenol. *J Material Sci Eng* 2016;5:223.
35. Ines BS et al. Effects of Irrigations with Treated Municipal Wastewater on Phenological Parameters of Tetraploid *Cenchrus ciliaris L.* *J Food Process Technol* 2016;7:553.
36. Yoshida J et al. Black Tea Polyphenols Suppress Postprandial Hyperglycemia In Vivo in Mice and Inhibit α -Glucosidase Activity *In Vitro*. *J Metabolic Synd* 2015;5:194.
37. de Jesus Marques E et al. Occurrence and Distribution of Polyphenolics in *Species of Deguelia* Leguminosae. *J Microb Biochem Technol* 2015;7:327-333.
38. Karar MGE and Kuhnert N. UPLC-ESI-Q-TOF-MS/MS Characterization of Phenolics from Crataegus monogyna and Crataegus laevigata Hawthorn Leaves, Fruits and their Herbal Derived Drops Crataegutt Tropfen. *J Chem Biol Ther* 2015;1:102.
39. Wu Y et al. A DFT Study on the Degradation of Chlorobenzene to p-chlorophenol via Stable Hydroxo Intermediate Promoted by Iron and Manganese Monoxides. *J Phys Chem Biophys* 2015;5:196.
40. Al-Musharfi NK et al. Comparison of Ascorbic Acid, Total Phenolic Content and Antioxidant Activities of Fresh Juices of Six Fruits Grown in Oman. *J Food Process Technol* 2015;6:513.
41. Trivedi MK et al. 2015 Characterization of Physical, Thermal and Spectral Properties of Biofield Treated O-Aminophenol. *Pharm Anal Acta* 6:425.
42. Prasad CH et al. Catalytic Reduction of 4-Nitrophenol Using Biogenic Silver Nanoparticles Derived from Papaya *Carica papaya* Peel extract. *Ind Chem Open Access* 2015;1:104.
43. Trivedi MK et al. Biofield Treatment: An Effective Strategy for Modulating the Physical and Thermal Properties of O-Nitrophenol, M-Nitrophenol and P-Tertiary Butyl Phenol. *J Bioanal Biomed* 2015;7:156-163.

44. Shimelis D et al. Effects of Polyvinyl Pyrrolidone and Activated Charcoal to Control Effect of Phenolic Oxidation on In Vitro Culture Establishment Stage of Micropropagation of Sugarcane *Saccharum Officinarum* L.. *Adv Crop Sci Tech* 2015;3:184.
45. Trivedi MK et al. Investigation of Isotopic Abundance Ratio of Biofield Treated Phenol Derivatives Using Gas Chromatography-Mass Spectrometry. *J Chromatograph Separat Techniq* 2015; S6:003.
46. Dundar A et al. Antioxidant, Antimicrobial, Cytotoxic and Anticholinesterase Activities of Seven Mushroom Species with their Phenolic Acid Composition. *J Horticulture* 2015;2:161.
47. Mariswamy VH et al. Imino-4-Methoxyphenol Thiazole Derived Schiff Base Ligands: Synthesis, Spectral Characterization and Antimicrobial Activity. *Chem Sci J* 2015;6:102.
48. Nath K et al. Role of Total Soluble Sugar, Phenols and Defense Related Enzymes in Relation to Banana Fruit Rot by *Lasiodiplodia theobromae* [Path. Griff. and Maubl.] During Ripening. *J Plant Pathol Microb* 2015;6:299.
49. Efferth T et al. Polyphenols-Versatile Weapons in Plants and Human Beings. *Med Aromat Plants* 2015;4:e159.
50. Abd El-Azim MHM et al. Phenolic Compounds and Cytotoxic Activities of Methanol Extract of Basil *Ocimum basilicum* L. *J Microb Biochem Technol* 2015;7:182-185.
51. Barber MS et al. Antimicrobial intermediates of the general phenylpropanoid and lignin specific pathways. *Phytochemistry* 2000;54:53–56.
52. Bauer A et al. Antibiotic susceptibility testing by a standardized single disk method. *Am J Clin Pathol* 1966;45:493–496.
53. Boudet A. Evolution and current status of research in phenolic compounds. *Phytochemistry* 2006 ;68:2722–2735.
54. Dixon RA. Natural products and plant disease resistance. *Nature* 2001;411:843–847.
55. Jeandet P et al. Phytoalexins from the Vitaceae: biosynthesis, phytoalexin gene expression in transgenic plants, antifungal activity, and metabolism. *J Agric Food Chem* 2002;50:2731–2741.
56. Kuzina LV et al. In vitro activities of antibiotics and antimicrobial peptides against the plant pathogenic bacterium *Xylella fastidiosa*. *Lett Appl Microbiol* 2006;42:514–520.
57. Taguri T et al. Antimicrobial activity of 10 different plant polyphenols against bacteria causing food-borne disease. *Biol Pharm Bull* 2004; 27:1965–1969.
58. Taguri T et al. Antibacterial spectrum of plant polyphenols and extracts depending upon hydroxyphenyl structure. *Biol Pharm Bull* 2006;29:2226–2235.
59. Fu L et al., “Antioxidant capacities and total phenolic contents of 62 fruits,” *Food Chemistry* 2011;129pp. 345–350.
60. Arakawa H et al. Antibacterial activities of persimmon extracts relate with their hydrogen peroxide concentration. *Biological and Pharmaceutical Bulletin* 2014;37:1119–1123.
61. Mullen W et al. Evaluation of phenolic compounds in commercial fruit juices and fruit drinks. *Journal of Agricultural and Food Chemistry* 2007;55:3148–3157.
62. Zhao J et al. Antimicrobial activities of some thymol derivatives from the roots of *Inula hupehensis*. *Food Chemistry* 2010;120:512–516.
63. Benzie IFF and Szeto YT. Total antioxidant capacity of teas by the ferric reducing/antioxidant power assay. *Journal of Agricultural and Food Chemistry* 1999;47:633–636.
64. Re R et al. “Antioxidant activity applying an improved ABTS radical cation decolorization assay. *Free Radical Biology and Medicine* 1999;26:1231–1237.
65. Borges A et al. Antibacterial activity and mode of action of ferulic and gallic acids against pathogenic bacteria. *Microbial Drug Resistance* 2013;19:256–265.
66. Cerda-Carrasco ADL et al. Phenolic composition and antioxidant capacity of pomaces from four grape varieties *Vitis vinifera* L. *J Sci Food Agricult* 2015 ;957:1521–1527.
67. Darra NE et al. A Comparative study on antiradical and antimicrobial properties of red grapes extracts obtained from different *Vitis vinifera* varieties. *Food Nutr Sci* 2012;3:1420–1432.

68. Doshi P et al. Phenolic composition and antioxidant activity in grapevine parts and berries *Vitis vinifera L.* cv. Kishmish Chornyi Sharad Seedless during maturation. *Int J Food Sci Technol* 2006;41:1–9.
69. Giusti MM, and Wrolstad RE. Anthocyanins: characterization and measurement with UV-visible spectroscopy. 2001;F1.2.1–F1.213 in R. E. Wrolstad, ed. *Current protocols in food analytical chemistry*. Wiley, New York.
70. González-Centeno MR et al. Characterization of polyphenols and antioxidant potential of white grape pomace byproducts *Vitis vinifera L.* *J Agricult Food Chem* 2013; 61:11579–11587.
71. Makkar HPS et al. Gravimetric determination of tannins and their correlations with chemical and protein precipitation methods. *J Sci Food Agric* 1993;61:161–165.
72. Nile SH et al. Polyphenolic contents and antioxidant properties of different grape *V. vinifera*, *V. labrusca*, and *V.* hybrid cultivars. *BioMed Res Int* 2013; 718065.
73. Nittiema LW et al.. In vitro antimicrobial activity of some phenolic compounds coumarin and quercetin against gastroenteritis bacterial strains. *Int J Microbiol Res* 2012;3:183–187.
74. Oliveira DA et al. Antimicrobial activity and composition profile of grape *Vitis vinifera* pomace extracts obtained by supercritical fluids. *J Biotechnol* 2013;164:423–432.
75. Ozkan GO et al. Antioxidant and antibacterial activities of *Rosa damascena* flower extracts. *Food Sci Technol Int* 2004b ;10:277–281
76. Porter LJ et al. The conversion of procyanidins and prodelphinidins to cyanidin and delphinidin. *Phytochemistry* 1986;25:223–230.
77. Pettit S and Scully C. Polyphenols, oral health and disease: A review *J Dent* 2009;376:413–423.
78. Puupponen-Pimia RL et al. Antimicrobial properties of phenolic compounds from berries. *J Appl Microbiol* 2001;90:494–507.
79. Ramirez-Lopez LM et al. Analysis of phenolic compounds in commercial dried grape pomace by high-performance liquid chromatography electrospray ionization mass spectrometry. *Food Sci Nutr* 2014; 2:470–477.
80. Re R et al. Antioxidant activity applying an improved ABTS radical cation decolorization assay. *Free Radic Biol Med* 1999;26:1231–1237.
81. Samatha TR et al. Quantification of total phenolic and total flavonoid contents in extracts of *Oroxylum Indicum L.* Kurz. *Asian J Pharm Clin Res* 2012;5:177–179.
82. Sánchez-Moreno C et al. A procedure to measure the antiradical efficiency of polyphenols. *J Sci Food Agric* 1998;76:270–276.
83. Smith-Palmer AJ et al. Antimicrobial properties of plant essential oils and essences against five important food-borne pathogens. *Lett Appl Microbiol* 1998;26:118–122.
84. Tabart JC et al. Comparative antioxidant capacities of phenolic compounds measured by various tests. *Food Chem* 2009;113:1226–1233.
85. Teixeira AN et al. Natural bioactive compounds from winery by-products as health promoters: a review. *Int J Mol Sci* 2014;15:15638–15678.
86. Vuorinen HK et al. Content of the flavonols myricetin, quercetin, and kaempferol in Finnish berry wines. *J. Agricult. Food Chem* 2000;48:2675–2680.
87. Barros L et al. Phenolic acids determination by HPLC-DAD-ESI/MS in sixteen different Portuguese wild mushrooms species. *Food Chem Toxicol* 2009;47: 1076–1079.
88. Cosgrove SE and Carmeli Y. The impact of antimicrobial resistance on health and economic outcomes. *Clin Infect Dis* 2003 ;36:1433–1437.
89. Khalafi-Nezhad A et al. Design, synthesis, antibacterial and QSAR studies of benzimidazole and imidazole chloroaryloxyalkyl derivatives. *Bioorg Med Chem* 2005;13: 1931–1938

90. Kim MY et al. Phenolic compound concentration and antioxidant activities of edible and medicinal mushrooms from Korea. *J Agric Food Chem* 2008;56: 7265–7270
91. Ozen T et al. Screening of antioxidant, antimicrobial activities and chemical contents of edible mushrooms wildly grown in the Black Sea region of Turkey. *Comb Chem High Throughput Screen* 2011;14: 72–84.
92. Stevanovic T et al. Bioactive Polyphenols from Healthy Diets and Forest Biomass. *Current Nutrition & Food Science* 2009;5: 264-295.
93. Essawi T and Srour M Screening of some Palestinian medicinal plants for antibacterial activity. *J Ethnopharmacol* 2000;70: 343-349.
94. Mulyaningsih S et al. Synergistic properties of the terpenoidsaromadendrene and 1,8-cineole from the essential oil of *Eucalyptus globulus* against antibiotic-susceptible and antibiotic-resistant pathogens. *Phytomedicine* 2010;17: 1061-1066.
95. Tsuchiya H et al. Comparative study on the antibacterial activity of phytochemical flavanones against methicillin-resistant *Staphylococcus aureus*. *J Ethnopharmacol* 1996;50: 27-34.
96. Bakkali F et al. Biological effects of essential oils – A review. *Food and Chemical Toxicology* 2008;46: 446-475.
97. Iriti M and Faoro F. Chemical Diversity and Defence Metabolism: How Plants Cope with Pathogens and Ozone Pollution. *Int J MolSci* 2009;10: 3371-3399.
98. Rice-Evans CA et al. Structure-antioxidant activity relationships of flavonoids and phenolic acids. *Free RadicBiol Med* 1996;20: 933-956.
99. Välimäa et al. Antimicrobial and cytotoxic knotwood extracts and related pure compounds and their effects on food-associated microorganisms. *Int J Food Microbiol* 2007;115: 235-243.