Chapter 1

Introduction

The protection of an oxidisable material against atmospheric aging and degradation is a pre-requisite for their successful technological development and their applications.

It is well established that free radicals play a major role in the occurrence of tissue damage at the site of inflammation. As a consequence it might be possible to diminish tissue damage on treatment with effective radical scavengers[1]. Many pharmaceuticals are prone to auto-oxidation, a free radical reaction initiated by UV radiation in the presence of a trace amount of oxygen. The addition of small amount of an antioxidant inhibits the formation of highly reactive free radicals and the chain reaction by providing a hydrogen atom or an electron to the free radical.

Fundamentally, there are various means available to retard oxidation and the resultant stabilization, of which addition of antioxidants is the most commonly used method. Although plastics such as polyvinyl chloride (PVC), polyethylene (PE) and polystyrene (PS) have been produced on a large scale for more than fifty years, the efforts in research and development in the additive field are still quite intensive[2].

Antioxidants are natural or synthetic substances that can delay or lower the rate of oxidation reactions of oxidisable materials by interactions with free radical chain reactions or by suppressing the formation of free radicals in the oxidation processes.

The most important process in foods and other lipid containing materials (pharmaceuticals, cosmetics, fodders) is auto-oxidation, i.e. the reaction with molecular (triplet) oxygen. Besides auto-oxidation, oxidation with singlet oxygen, peroxide, ozone, metals and other oxidising agents may occur. All these reactions lead to development of off-flavours, off-odours termed rancid, shortening of their shelf life and rendering the material unacceptable. Oxidative reactions decrease nutritional quality and certain oxidation products are potentially toxic.

Organic material has a strong tendency to react with oxygen and oxidise. This is true for most of the commercial organic materials e.g. plastics, elastomers, fibres, fuels, lubricants, foods and drugs. The concept of antioxidant and the discovery that small amount of reducing agent could protect material susceptible to oxidation were attributed to S. L. Biglow (1898).[3]

Oxidation of organic material takes place by a number of processes,[4]
1) Auto-oxidation 2) Bio-oxidation 3) Combustion 4) Photo-oxidation.
The ultimate result of these processes is the conversion of carbon and hydrogen in to carbon dioxide and water.

The mechanism by which an organic material (RH) undergoes oxidation involves a free radical chain reaction.

Initiation:

$RH \longrightarrow$ Free radicals $R\bullet, ROO\bullet, RO\bullet, HO\bullet$ --------1

$ROOH \longrightarrow RO\bullet + HO\bullet$

$ROOH \longrightarrow 2RO\bullet$

$2ROOH \longrightarrow RO\bullet + ROO\bullet + H_2O$ ---------------2

Propagation:

$R\bullet + O_2 \longrightarrow ROO\bullet$ -----3

$ROO\bullet + RH \longrightarrow ROOH + R\bullet$ ---------------------4

Termination:

$2R\cdot \longrightarrow R\text{-}R$ ---------------------------5

$ROO\cdot + R\cdot \longrightarrow ROOR$ -----------------------------------6

$2ROO\cdot \longrightarrow$ Non radical products R-O-O-R+ O_2 ---------7

Equation 1 is important only during the very early stage of auto-oxidation. Radicals formed here gradually produce hydroperoxides,[5] which become the kinetically important inhibitors. Possible examples of early inhibition steps include stress induced bond rupture as in polymer processing and fatigue,[6-9] bimolecular reaction of hydrocarbon with oxygen[10] and various photochemical processes[11].

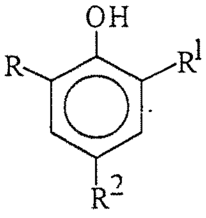
Auto-oxidation can be inhibited at the initiation and propagation steps. Antioxidants are often classified on the basis of their ability to do either or both.

Two general classifications can be made to categorise antioxidants.

1) Primary (Chain terminating) antioxidants.
2) Secondary (Peroxide decomposing) antioxidants.

[1] Primary antioxidants

Antioxidant that interrupts the propagation step (Eq. 3.) markedly reduces the oxidation rate. The most important commercial antioxidants that function in this way are hindered phenols and secondary alkyl, aryl and diaryl amines. e.g. structure **1** represents the important class of propagation inhibitors.



R = R1=R2 = Alkyl (Same or Different)
R=R1= Tert-butyl

1

They act as primary antioxidants by donating their reactive hydrogen (O-H, N-H) to free radicals, particularly to peroxy radicals.

$$ROO\bullet + AH \longrightarrow ROOH + A\bullet$$

AH =Hydrogen donating antioxidant

To sufficiently terminate the oxidative process, the antioxidant radical ($A^{\cdot}$) must be rendered stable to prevent the continuation of propagation of new radicals. These radicals, in most cases, are stabilized via their electron delocalisation or resonance, as is indicated in case of hindered phenolics like 2,6-di-tert-butyl-4-methyl phenol (BHT)[12] (Figure 1.1).

(a) Phenolic antioxidants

Hindered phenols are major class of antioxidants and are presently used as radical trapping agents in plastics, elastomers, synthetic fibres, fuels, lubricants and foods. Steric hindrance is provided by bulky substituents in the position on the ring ortho to hydroxyl group and they also influence the specificity of the phenols by blocking phenoxy radicals from abstracting hydrogen atom from organic substrates. Phenolic antioxidants can further be categorised into the forms showed in Figure 1.2. Simple phenolics **2**, Bis phenolics **3**, Poly phenolics **4**, Thiobis phenolics **5** (Figure 1.2).

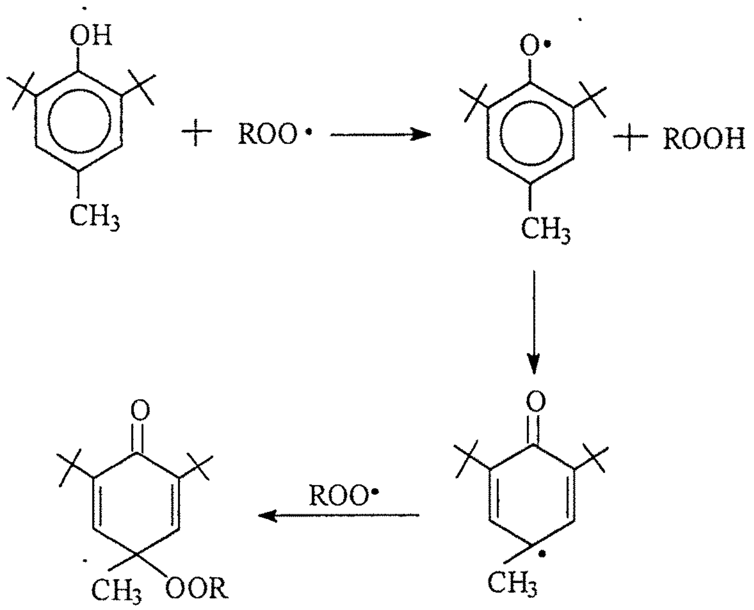
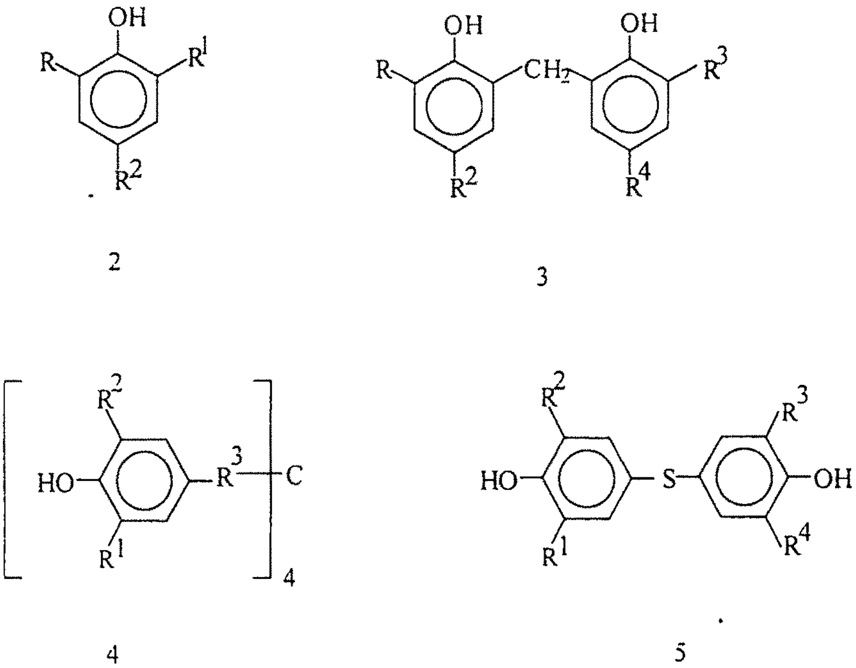


Figure 1.1 : The chain termination mechanism of BHT,
A hindered phenolic

(b) Amines

Secondary aryl amines (Figure 1.3) function by hydrogen donation similar to the phenols. However, at higher temperature, they are also capable of decomposing peroxides[13]. Although members of the amine class of primary antioxidants are usually more effective than the chain terminator and peroxide decomposers, there are limited applications in which their discolouring characteristic can be tolerated or masked. Amines are widely used in unsaturated polymers containing carbon black. Examples of this class of antioxidants are: diphenyl amine **6**, N,N'-diphenyl- p-phenylene diamine **7**, phenothiazine **8** (Figure 1.4).



2 3 4 5

Figure 1.2 : Hindered phenolic types

Simple phenolics 2, bisphenolics 3, polyphenolics 4, thiobisphenolics

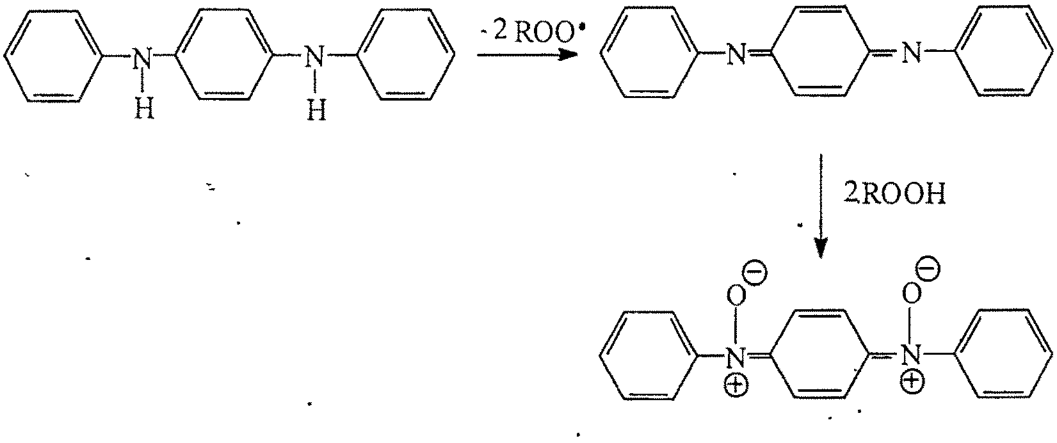
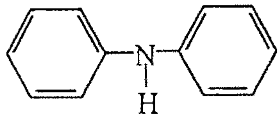


Fig 1.3 Antioxidant mechanism of secondary aryl amines



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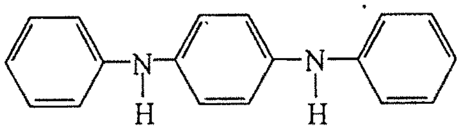

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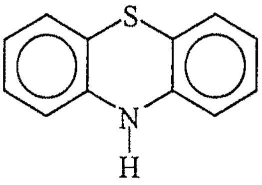

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Figure 1.4 : Examples of Amine antioxidants

[2] Secondary Antioxidants

This class of antioxidants consists of various trivalent phosphorus and divalent sulphur containing compounds, most notable of which are organophosphites and thioesters. The secondary antioxidants are also termed as preventive stabilizers, because they prevent the proliferation of alkoxy and hydroxy radicals by destroying hydroperoxides. Two main classes of antioxidants inhibit the initiation step in themal oxidation[14]

(a) ***The peroxide decomposers***

Antioxidant that decompose hydroperoxide include sulphide, such as dialkyl thiodipropionate **9**, aryl phosphite **10**, and metal salts of certain dithioacids such as zinc dithiocarbamate **11**, xanthate **12**, and dithiophosphate **13.**[15-17] (Figure 1.5)

Phosphites function by reducing hydroperoxide to alcohols and thus converting themselves to phosphates.

$$(ArO)_3P + ROOH \longrightarrow ROH + (ArO)_3P{=}O$$

Among the phosphites, most popular stabiliser is tris (nonyl phenyl) phosphite (TNPP). A serious drawback of phosphite is its sensitivity to hydrolysis. Hydrolysis of phosphite ultimately leads to the formation of **phosphorus** acid, which can cause corrosion of processing equipment.

$(RO_2CCH_2CH_2)_2S$
9

$(RO)_3P$
10

$(R_2NCS_2)_2Zn$
11

$(ROCS_2)_2Zn$
12

$[(RO)_2PS_2]_2Zn$
13

Figure 1.5 : Examples of peroxide decomposers

(b) Metal deactivators: (Preventive Antioxidants)

Deactivators can inhibit the ability of metal ion catalysed oxidation.[18] Homolytic decomposition of hydroperoxide is catalysed by traces of metal ion which are capable of undergoing one electron oxidation-reduction reactions. (Eqs. 8,9)[19-22]

$$ROOH + M^{n+} \longrightarrow R\dot{O} + M^{(n+1)+} + OH^{-} \text{-------} \ 8$$

$$ROOH + M^{(n+1)+} \longrightarrow RO\dot{O} + M^{n+} + H^{+} \text{-------} \ 9$$

These additives chelate metal ions and increase the potential difference between the oxidised and reduced states of metal ion to produce radical from hydroperoxide by oxidation and reduction.

The deactivation of metal ions by chelation operates by

(i) Steric effect which blocks the hydroperoxide from the co-ordination site on the metal ion.

(ii) An electronic effect which preferentially stabilize one of the metal oxidation states.[18]

However, chelation is not always effective and can sometimes enhance metal ion activity. The most effective metal ion deactivators are often polydentate chelating agents capable of forming very stable chelates in which all the coordination sites are occupied.[18.23]

Examples of commercial metal deactivators used in polymers are oxallyl bis (benzylidene hydrazide) **14**, N,N'-bis-(3,5-di-tert-butyl-4-hydroxyhydro cinnamoyl) hydrazine **15**, 2,2'-oxamido bis ethyl (3,5-di-tert-butyl-4-hydroxy) hydro cinnamate **16**, and ethylene diamine tetra acetic acid **17** and its sodium salt. (Figure 1.6).

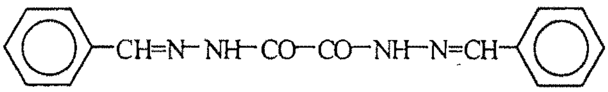
Photo-oxidation and Stabilisation

Hydroperoxides are important in photo-oxidation. They are decomposed by solar radiation both photochemically and thermally. A number of photochemical reactions can produce hydroperoxides early in the photo-oxidation process.

$$ROOH \longrightarrow RO^{\cdot} + {}^{\cdot}OH \quad \text{--} 10$$

These include radical production from hydrocarbon oxygen transfer complexes,[24] Norrish scission of photoexcited carbonyl,[25] scission through photoexcited conjugated and isolated double bonds[26] and from photoexcited catalyst residues.[27] Hydroperoxides can also form directly through an "ene" reaction of olefins with photochemically generated singlet oxygen.[28] Therefore, agents that protect substrates from photo-oxidation include those that reduce the amount of damaging radiation entering the substrate (UV absorber) and those which deactivate photoexcited chromophore by energy transfer (quenching agents).

Most of the hindered phenols alone provide little protection, probably because they are rapidly decomposed under UV irradiation.[29,30] Nevertheless, combination of UV absorbers (qv) and phenolic antioxidants can be synergistic and are commercially important.



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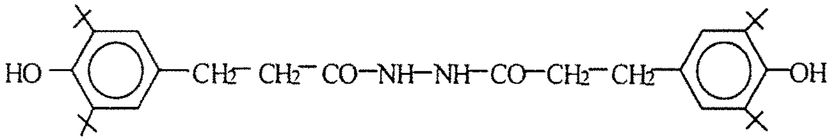

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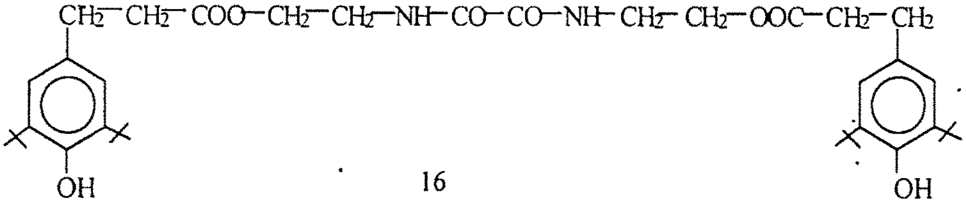

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$_2(HOOCH_2C)N-CH_2-CH_2-N(CH_2COOH)_2$

17

Figure 1.6 : Examples of metal deactivators

Aryl benzofuranone (Lactone) antioxidants[31]

Revolutionary stabilisation chemistry has been developed based on the aryl benzofuranone moiety. The primary role of lactone moiety is a hydrogen atom donation to a carbon-centered free radical, followed by scavenging of carbon centered free radical by the benzofuranyl radical. The use of an aryl benzofuranone in combination with traditional stabilisers (phenolic and phosphite) affords a system that can be used to preserve the material during its life cycle in a cost effective fashion. A very small amount of lactone is sufficient under the very harsh processing conditions. (Figure 1.7)

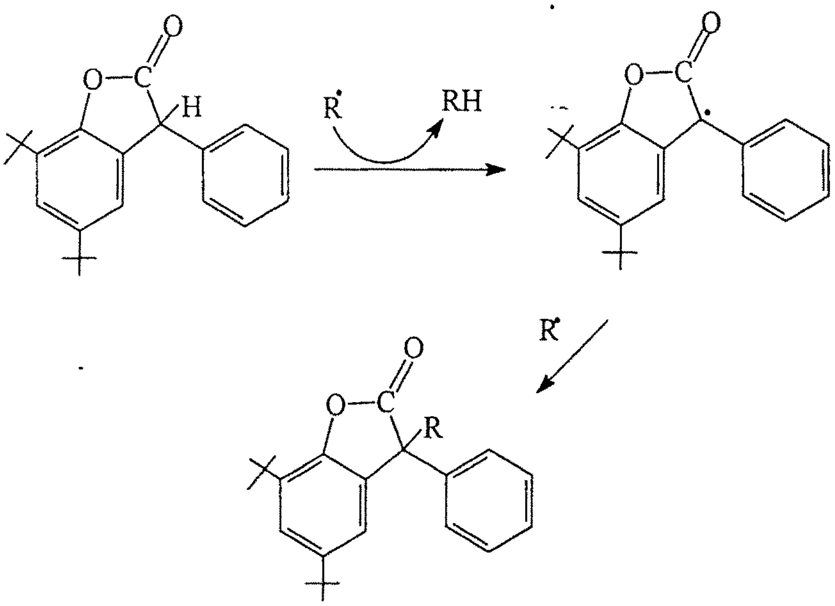


Figure 1.7 : Free radical trapping mechanism of aryl benzofuranone

Hydroxylamine antioxidants[31]

Novel. stabilisation chemistry has recently been developed based on hydroxylamine moiety. The primary role of the hydroxyl amine moiety is a hydrogen atom donation to an oxygen centered free radical followed by a second hydrogen donation by the nitroxyl radical. A secondary mode of extended reactivity is achieved via carbon centered free scavenging by the nitrone transformation product. (Figure 1.8)

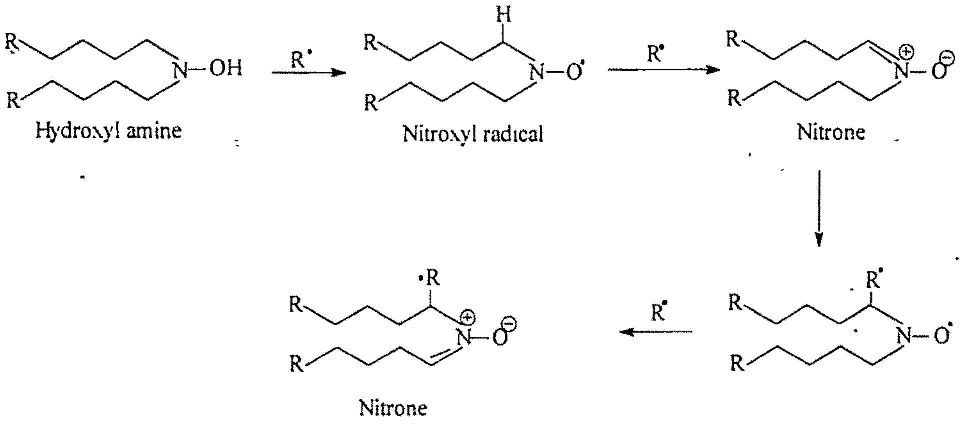
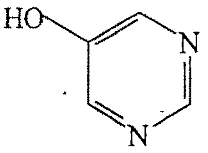


Figure 1.8 : Multiple equivalents of stabilization via N-OH.

A new family of heterocyclic antioxidants based on 5-pyrimidinols has been developed by *Pratt et al*[32]. They have proved that ionisation potential increased significantly as a function of nitrogen substitution in aromatic ring. They have observed that reaction rate of pyrimidinols with alkyl and peroxy radicals were greater than those measured with phenolic compounds.



5-Pyrimidinol

Bound antioxidants

The chemical bonding of antioxidant onto polymer molecule prevents migration and the accompanying loss of stabilizers (Figure 1.9). Antioxidants bound in this way would not be lost either through evaporation or solvent extraction. Antioxidants which are co-polymerized in to the elastomer chain have also been developed.[33] Unexpected advantage of bound antioxidants has been observed due to selective protection of most oxidatively sensitive resins of the polymers in rubber modified polymer blends. The product formed in the following reaction is a typical sec-alkylamino diphenylamine which is characteristic of the best rubber antidetergents.[34]

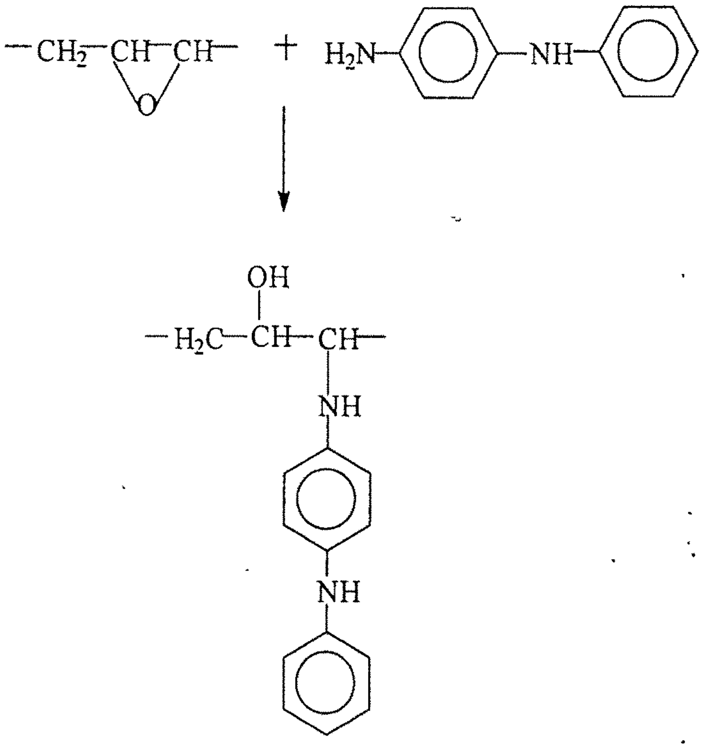


Figure 1.9

Antioxidant combinations

It is possible to obtain a high level of protection by using combinations of two or more different stabilizers. In thermal oxidation the proper selection of antioxidants can provide very high level of protection. Combination of antioxidants may result in I) À simple additive effect, II) antagonism III) synergism.

I) *Additive effect*

Usually when two or more antioxidants of the chain breaking type are used in combination, it results in simple additive effect. This effect, however, may exceed that obtained when the concentration of either component is increased two folds. Two or more chain breaking antioxidants could provide better retention than higher concentration of either component. The combination of short term or processing antioxidants with one design for long term protection would be an example of such a combination.

II) *Antagonistic effect*:

Antagonism between antioxidants would be expected if interactions occur which would destroy or reduce the effectiveness of either component. *Hawkins and co-workers*[35] observed an antagonistic effect when carbon black, used to protect against outdoor weathering, was combined with secondary amines or certain hindered phenols.

III) *Synergism*

When combination of two or more antioxidants provide more protection than would be expected from the sum of that provided by the individual components, the phenomenon is referred to as synergism.

The most common synergistic combinations are mixtures of antioxidants operating by different mechanisms. For example combination of peroxide decomposer with propagation inhibitors is used in certain elastomers.

When a synergistic combination consists of two or more antioxidants, each functioning by the same mechanism but of an unequal activity, the phenomenon has been referred to as homosynergism.[36]

Homosynergism

If AH is a highly reactive hindered phenol and A'H a less hindered phenol, hydrogen abstraction by peroxy radicals is particularly fast with A'H. The phenoxy radical A` is rather reactive and may participate in chain transfer reaction such as given below (Eqs. 11, 12). In the presence of more hindered phenols AH, A` radical also enter the exchange reaction. (Eq. 13).[37]

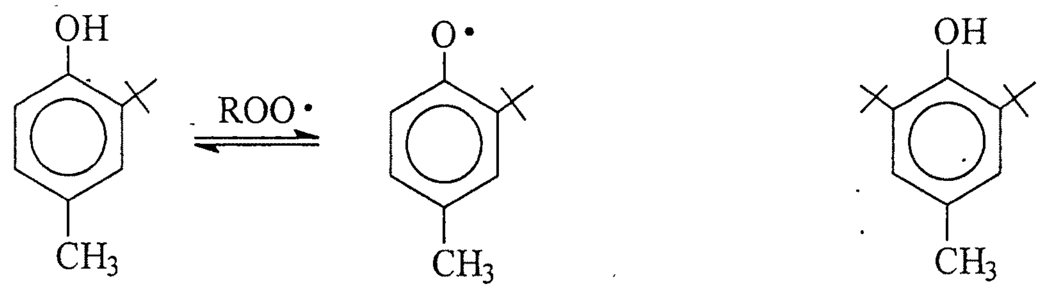
$$A'^{\bullet} + RH \longrightarrow A'H + R^{\bullet} \text{ ———— } 11$$

$$A'^{\bullet} + ROOH \longrightarrow A'^{\bullet} + ROO^{\bullet} \text{ ———— } 12$$

$$A'^{\bullet} + AH \longrightarrow A'H + A^{\bullet} \text{ ———— } 13$$

In equation 13 equilibrium is displaced to the right hand side, because the highly hindered phenoxy radical A is less reactive than less hindered phenoxy radical $A'^{\bullet}$.

Homosynergism has been observed with combination of two hindered phenols acting as chain-breaking antioxidants[38] (Figure 1.10). The more effective phenol (I) is the primary deactivator of propagating radicals. The less reactive phenol (II) acts as a reservoir for labile hydrogen to regenerate the primary antioxidant. Here two phenols differ in the size and number of the ortho substitutents, which effect the ease of hydrogen abstraction. Phenol (I) has less hindrance adjacent to the labile hydrogen and is therefore more effective. Since it is regenerated from its radical by abstraction of hydrogen from (II), it is not depleted as rapidly.



I

II

Figure 1.10

Heterosynergism[39]

Heterosynergism arises due to the cooperative effect between mechanistically different class of antioxidants, i.e. combined effects of chain breaking and peroxide decomposers.

Powerful synergism is achieved in the melt and thermal stabilisation of polypropylene by using combination of hindered phenol and phosphite or phosphinite and sulphur compounds. Phosphite or phosphinite enhance the melt stabilising effect of hindered phenol and reduce discoloration of the polymers caused by the phenol transformation products. The cooperative effect of hindered phenols and phosphites occurs through two steps, whereby phenols scavenge alkyl phenoxy radical and phosphites decompose peroxides in a nonradical reaction which lead to enhanced melt stability of the polymer. Further interaction between the coloured transformation products of phenol and the phosphite antioxidant results in non-coloured products, hence a decrease in the extent of polymer discolouration (Figure 1.11).

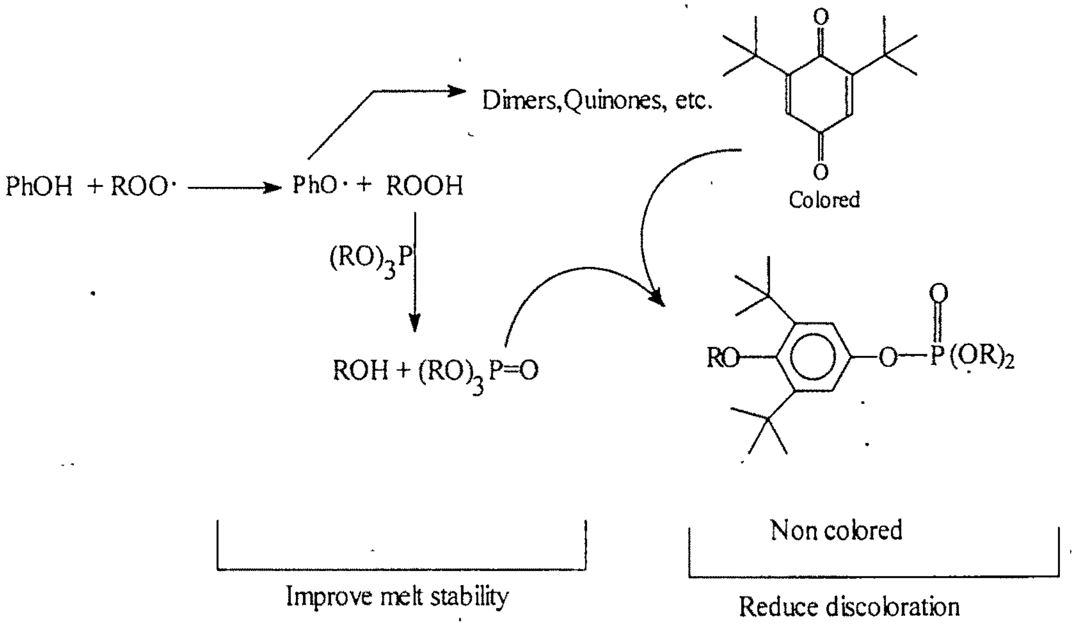


Figure 1.11

Similarly synergism between hindered phenols and sulfur compounds in polypropylene has been shown to occur due to the several cooperative reactions between them.

Autosynergism[4]

When two different antioxidant functions are present in the same molecule, then the effect of synergism observed is known as autosynergism. Here mechanism of action of both the antioxidants is same but they belong to the different class of chemistry.

Most commonly used synergistic combination of this type is a combination of hindered phenol and hindered amine. The free radical scavenging chemistry of phenolic antioxidant is hydrogen atom donation to oxygen centered radicals followed by oxygen centered radical scavenging of phenoxy radical. The bulky substituents influence the specificity of phenols by blocking phenoxy radicals from abstracting hydrogen atom from organic substrates. 2,6-Di-tert-butyl phenol is the widely used molecule in commercial hindered phenolic antioxidants.

Antioxidants derived from p-phenylene diamine and diphenylamine are highly effective peroxy radical scavengers. They are more effective than phenolic antioxidants for the stabilisation of easily oxidisable organic material, but most of them are coloured and formed highly coloured oxidation products. Thus their uses are generally limited to those for which discoloration is not a draw back. Secondary amine serves as a source of hydrogen atom that is abstracted by peroxy radicals to yield relatively stable aminyl radicals. The intermediate aminyl radicals have a low tendency to abstract hydrogen atom from organic materials. Tertiary amine showed no oxidation retarding properties but tertiary amine with some other functionality is widely used as commercial metal deactivator.

Applications of Antioxidants

Antioxidants are widely used in Elastomers, Plastics, Gasoline, Synthetic lubricant, Adhesive, Food products, Animal feed and Pharmaceuticals.[40] They are also used as anti-corrosive agents.

Plastics

The commercial success of most of the plastics depends on proper stabilisation by antioxidants or other additive incorporated by extrusion or of powder blends or by milling. Low density polyethylene used for making disposable garment bags does not require the use of antioxidants. A general purpose antioxidant, such as 2,6-di-tert-butyl-4-methyl phenol is adequate for low-density polyethylene. Relatively non-volatile polynuclear phenols, phenylene diamines or bis phenol sulphides are frequently used for electrical applications such as wire and cable insulation.

Polypropylene or Propylene copolymers are far more difficult to stabilise than polyethylene because of the presence of easily oxidisable tertiary hydrogen.

In general, antioxidants recommended for polypropylene and copolymers include phenolics, thiodipropionate, phosphite, phenylene diamines and dithiocarbamate.[41] Poly vinyl chloride (PVC) can be protected adequately with a wide variety of stabiliser systems that are comprised primarily of acid acceptor such as metallic soaps.[42] Other important plastics are stabilised by a variety of systems: Impact polystyrene is best protected with BHT. Although acrylonitrile butadiene-styrene (ABS) is produced in a smaller volume[43] than any of the four resins, the total antioxidant requirement is largest.[44]

Sterically hindered amines have been used as stabilisers against thermal oxidation of low-density polyethylene at high temperature as reported by *Dobrescu and co-workers.*[45]

Boehshar and co-workers[46] synthesised tetra kis (2,4-di-tert butyl phenyl)-4,4'-bis-phenylene diphosphonite and used as a stabiliser for polypropylene.

Chemeta et al.[47] reported the use of organic phosphites combined with hindered amine light stabilisers (HALS) as stabilisers in the photo and thermal oxidation of isotactic polypropylene.

3-Phenyl benzofuran-3-ones prepared by reaction of mandelic acid with 2-(1-hexadecylethyl) phenols at low pressure were used as polymer stabilisers by *Dubs and Pitteloud.*[48]

Elastomers

The use of antioxidants in raw and cured rubber is essential in order to retard oxidative deterioration promoted by heat, light, and oxygen. Styrene-butadiene rubber (SBR) must be protected with antioxidants in the polymerisation step. This ensures easy processing, good storage stability and high quality cured end products. Phosphites and p-phenylene diamines are used as stabilisers for both SBR and butyl rubber. Cured and uncured rubbers insufficiently protected with antioxidants differ considerably in the manner by which they degrade oxidatively. Isoprene and butyl rubber soften by chain scission or depolymerisation, where as SBR, neoprene, butadiene and acrylonitrile become stiff and brittle because of cross-linking or polymerisation. However, there are speciality antioxidants, such as mercaptobenzimidazole for nitrile rubber and nickel dimethyl dithiocarbamate for epichlorohydrin rubber. In general, phenolics are not used in cure recipies for dry rubber because of their low activity. However, they are employed when minimum discoloration is required. Diphenylamine and phenylenediamine types are particularly important because of their ability to retard fatigue or flex cracking in tires and belts.

According to *Babayan et al.*[49] the heat resistance to rubber based composition could be improved by the use of N,N'-bis-(3,5-di-tert-butyl-4-hydroxy benzyl)methyl-amine.

Gasoline

Unprotected, stored gasoline discolours slowly and gums are deposited because of oxidation and polymerisation. Gasoline containing such gum causes valve sticking, plugged fuel jets and in general, lowered motor efficiency. The effect of copper on gasoline is particularly deleterious since only trace amount promotes oxidation viz. peroxide decomposition. The combination of an antioxidant capable of decomposing peroxide and metal deactivators is the prime requisites for optimum stabilisation of gasoline. BHT and N,N' di-sec-butyl-p-phenylene diamine are widely used for gasoline. The salicylidene is an effective copper inhibitor for gasoline.

α-Methyl benzylidene octadecylamine as antiwear and antioxidant for hydrocarbon fuel was reported by *Bebikh et al.*[50]

Morris and co-workers[51] showed the effects of stabiliser additives on the thermal stability of jet fuel. The behaviour of several types of fuel stabilisers like phenylenediamine, an aliphatic tertiary amine and metal deactivator was examined in the thermal stress of jet fuels in modified JETOT.

Lubricants

Lubricants and lubricating oils are the most important class of material, which require antioxidant protection. Many of them function at high temperature and are best protected by phenolic and aromatic amine antioxidants such as dioctyl diphenylamine and phenyl-α-napthylamine. Hydraulic fuels are protected by phenolic antioxidants such as BHT or aromatic amine. Synergistic effect is also obtained by mixture of antioxidants. At the same time gear oils are protected by sulphur or sulphur- phosphorus containing additives although at a greater concentration. greases are protected by phenolic amine or multipurpose sulphur containing compounds such as metal dialkyldithio carbamate. Gasoline or diesel engine oils are protected by zincdithiophosphate.

Dibase and co-workers[52] reported that sulphur containing compounds are useful as general purpose antioxidants and friction modifiers for lubricating compounds and automatic transmission fluids and additive especially in metal working lubricants. They prepared lubricants by sulphurising fatty acid esters of a polyhydric alcohol.

Cardis and co-workers[53] reported alkyl benzene sulfonyl derivatives of N,N'-diorganodithiocarbamic acid as multifunctional additives for lubricating oils.

Adhesive

The water-based adhesives may be formulated with polymers such as acrylate and carboxylated neoprene, which have good inert stability. Hot melts are subjected to decomposition as evidenced by the development of discoloration, skinning, charring or change in viscosity. The ideal antioxidant should maintain the original properties of a hot-melt and also be thermally stable permanent non-toxic and meet FDA requirements. Phenolic antioxidants and phosphites or blends are apparently preferred for the majority of hot-melt systems. Tri and tetra functional phenolic antioxidants have been developed for less stable polyolefin systems such as polypropylene based hot melts. The losses of antioxidants from hot melts emphasize the need for new types of antioxidants.

Food products

Flavours and order of many foods deteriorate rapidly in the presence of oxygen. Again, the flavour and odour of carbonyl compounds derived from auto-oxidation of food lipids are perceived as rancid. The selection of the antioxidant is based on the substract, its method of preparation, packing and distribution. It is important that the antioxidant is added to the fats and oils or intact food before oxidation has started. Antioxidants in cooking oils are used primarily for their carry through and stabilising effect on the fried product. This property of carry through is essential for the success of several commercial fried foods.[54] The most widely used antioxidant in food is BHT. Moreover synergism with mixture of antioxidants is frequently demonstrated[55] and standard commercial synergistic mixtures are available. Many of them also contain chelating agent such as citric acid for metal ions in fats and in oils or sodium tripolyphosphate for meat system.[56,57] *Chiba and co-workers*[58] reported the use of organic acid, salts of amino alcohols $[RCH(NH_3)^+(CH_2OH)]A^-$ (R= lower alkyl, A= organic anion) as highly effective for oils and oily foods. They are highly thermostable and non-toxic compared with other conventional antioxidants.

Noor and Augustin[59] reported the effectiveness of antioxidants on the stability of banana chips. The effectiveness of BHA and BHT in improving the stability of banana chips stored at 65^{0}C was compared. Chips fried in refined bleached and deodorised (RBD) olein containing BHA or BHT was reported to be more stable than chips fried in RBD olein without antioxidant. Antioxidants for foods and edibles have also been reported by *Sree and Lal*[60], who used BHT to stabilise ghee during its clarification from butter and its storage.

Animal feed

Antioxidants are used in animal feeds to retard the oxidation of vitamins A and E, carotene, pigments and to stabilise rendered animal feed fats and vegetable oils commonly used to increase energy density. Codliver oil has been mixed with BHT to prevent the oxidation of vitamin A present in fish oil.[60a]

Biological applications

The most important application of antioxidants is in medical field. They are found to prevent the oxidative degradation of eye lens and cataract.[61] *Lam and co-workers*[62] have shown anti-tumor properties of 3,5-bis-(3,5-di-tert-butyl-4-hydroxybenzyl)-2,3,6-trimethyl benzyl derivatives. *Takashashi*[63] reported a decrease in blood coagulation by oral administration of BHT. *Meerson*[64] reported that BHT is effective in preventing heart damage due to acute over load.

Gannushkina and co-workers[65] have shown effectiveness of the versatile antioxidant BHT in reducing cerebral edema and cerebral ischema.

BHT has also been found to be potent inactivator of virus. *Reimund*[66] suggested that BHT disturbs the lipid envelope of virus, there by inhibiting its absorbance in host cell. This is a very important finding because virus responsible for AIDS contains a lipid envelope and BHT may prove to be an effective weapon against this dreaded disease. Naturally occurring antioxidants e.g. phenolic fraction extracted from Arenica foliosa has been found to be effective in reducing the damage to liver on large doses of tetracycline.[67]

The anti-carcinogenic properties of the synthetic phenolic antioxidants BHA and BHT were first reported by *Wattenberg*[68] in a study showing that 500 ppm in the diet, phenolics inhibited polycyclic aromatic hydrocarbon induced forestomach tumor in mice and mammary tumor in rats. BHT and BHA are effective in inhibiting chemically induced liver carcinogens at lower doses when the exposure to carcinogen is low.

Generation of Reactive Oxygen Species (ROS)[69]

The generation of ROS especially oxygen free radicals and hydrogen peroxide in body occur mainly by two processes.

(i) Accidental generation

This process includes mechanisms such as "leakage" of electron onto oxygen from mitochondrial electron transport chains, mitochondrial cytochrome P450 and their electron donating enzymes. This process also includes "auto-oxidation reactions" in which compounds such as catecholamine, ascorbic acid and reduced flavins react directly with oxygen to form superoxide. This auto-oxidation is usually catalyzed by the presence of transition metal ions.

(ii) Deliberate synthesis

The classical example of generation of ROS for useful purpose is that of activated phagocytes due to the oxidative burst. In addition, H_2O_2 is also generated in vivo by several oxidase enzyme such as glycolate oxidase, xanthine oxidase and delta amino acid oxidase. The plasma membrane compounds NADPH oxidase, lipo oxygenase and cyclo-oxygenase also produce ROS.

Besides these, the ROS also come from external sources such as ionising radiations, toxins, drugs, chemicals and environmental pollution. Global climate changes as a result of the so called green house effect and anthropogenic gas emissions (Chlorofluoro carbon), which cause stratospheric ozone depletion, are added threats.

Free radical mediated damage to Biomolecule

ROS damage biochemical processes, enzymes and genetic machinery because of their adverse interaction with biomolecules. The lipid peroxidations cause a reduction in membrane fluidity and permeability. ROS induced damage to proteins may result in fermentation, cross-linking, aggregation of protein and induction of auto-fluorescence. Many enzymatic processes are thus disturbed. At physiological P^H and temperature, auto-oxidation of monosaccharide such as glucose can produce hydrogen peroxide, peroxides and oxyaldehydes. Destruction and fragmentation of bases and deoxyribose sugar have been reported to occur following ROS attack on DNA. The resulting cyto-toxicity, mutations and potential for malignant change occur as a result of induced chromosomal aberrations.

The various diseases which have been oxidant stress are neurological, cardiovascular, degenerative disorder of eyes, drug or xanobiotics induced nephritic and gastrointestinal damage, cancer, inflammatory disease, aging, respiratory disorder and muscular disorder. The ROS can lead to significant cellular damage, therefore, in order to survive; aerobic organism has to develop antioxidant system to protect themselves.

Food or diet contains large number of antioxidants such as β-carotene, vitamin E, Se, Riboflavin and Zinc and all of them appear to play an important role in protecting the body against various diseases. The flavanoids, in which tea extracts are particularly rich are known to be scavenger of reactive oxygen species and free radicals. The scavenger effect of flavanoid has been proven for short-lived species such as singlet oxygen and superoxide, hydroxyl and peroxyl radicals as well as for stable species such as DPPH. Tea is a rich source of flavanoid that constitute 33% by dry weight of TEA. Therefore, currently there is much interest in tea as a source of antioxidants that can reduce the risk of cancer and cardiovascular diseases.

Role of antioxidant in biological system

The role of antioxidants are looked at from the point of view of preventing lipid oxidation, disease prevention, chemoprevention, mineral to protect against free radicals, protection of color loss in spices. Anti-mutagenic effect of antioxidants especially from a synergistic action leading to reducing the risk of muta disease like cardiovascular disease, cataract risk and other currently prevalent health problems.

Recenfly *Nair et al.*[70-73] reported the preparation of novel antioxidants based on hindered phenol in combination with acid hydrazone, thiosemicarbazone, oxadiazole and pyrazole. This combination gave active materials having the advantage of two or more stabilising moieties. The performance of the synthesised antioxidants was evaluated in isotactic polypropylene and was found to be comparable with that of commercially available antioxidants.

Sterically hindered phenols are the most important processing antioxidants amongst which BHT. Irganox 1010 and Irganox 1076 are the widely used. Hindered phenols. due to the formation of quinonoid transformation products during oxidation process, impart various degree of colour,the extent of which depends on their chemical structure.

Amine class of antioxidants is usually more effective than phenols because of their ability to act as chain terminator and peroxide decomposer. Their uses are generally limited to the applications in which their discolouring characteristic can be tolerated or masked.

Proposed work

By considering the various applications of hindered phenol and hindered amine as antioxidants, it was thought of interest to overcome the drawbacks of these antioxidants by modifying their structures. Present work deals with the synthesis of new antioxidants based on hindered phenol in combination with different stabilising moieties. This would give active materials having the advantage of more than one stabilising moiety. The performance of some of the synthesised antioxidants with polypropylene-copolymer and base fuel is evaluated.

Stabilisation efficiency of the synthesised antioxidants in polypropylene-copolymer is evaluated and compared with the commercial sample by using

1) Melt Mixing 2) Melt Flow Rate
3) Multiple extrusion and 4)Oxidative Induction Time

Antioxidant activity of the synthesised antioxidant in base fuel was performed by using Potential Residue Method.

Some of the synthesised antioxidants are screened for antibacterial activity on different bacteria by using Bore-well method.

The second chapter of the thesis deals with the synthesis and characterisation of antioxidants based on hindered phenol in combination with hindered amines, phosphine and olefinic linkage. Activity evaluation of synthesised antioxidants and comparison with commercial sample in base fuel is discussed.

The third chapter of the thesis consists of synthesis, characterisation and screening for antibacterial activity of antioxidants based on hindered phenol in combination with nitrogen and oxygen heterocyclics.

The Fourth chapter of the thesis comprises of synthesis and characterisation of Irganox – 1076 homologue by incorporating one more methylene group in alkyl chain. During the synthesis migration and de-tert-butylation of tert-butyl group was observed. The structure of Irganox-1076 homologue was modified by replacing octadecyl group with different alkyl groups. In this chapter synthesis and reactions of 1-(3',5'-di-tert-butyl-4'-hydroxyphenyl)-2-bromoethanone are also discussed.

The final chapter of the thesis deals with the evaluation of antioxidant activity of the synthesised antioxidants in polypropylene-copolymer using BHT as reference.

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