Summary

Antioxidants are used to retard the reaction of organic materials with atmospheric oxygen. Such reaction can cause variety of diseases including heart disease, aging and cancer; degradation of the mechanical and electrical properties of polymer; loss of flavour and development of rancidity in foods; and an increase in viscosity, acidity and formation of insolubles in lubricants. The role of antioxidants has received increased attention during past decades. Polyphenols are the important class of defence antioxidants and are widespread virtually in all plant foods. These include phenols, phenolic acids, flavanoids, tannins and lignans. The organic material undergoes auto-oxidation, which involves a free radical chain reaction. Free radical initiators are produced by several processes. Hydrogen donating antioxidants, such as hindered phenols and secondary aromatic amines, inhibit oxidation by competing with the organic substrate for peroxy radicals. 2,6-Di-tert-butyl phenol is the most widely used functionality in commercial hindered phenolic antioxidants. Substituents in the 4^{th} position influence the solubility of the antioxidants. Moreover, high molecular mass substituents influence the migration and extractability of antioxidants.

The present work was undertaken with a view to study some aspects of the antioxidants namely synthesis, characterisation and activity evaluation in search of better antioxidants. The study includes the synthesis of novel antioxidants based on hindered phenol in combination with various stabilising functionalities. Hindered phenol based antioxidants in combination with nitrogen and oxygen heterocyclics were screened for the biological activity. The antioxidant activity of some of the synthesised antioxidants is evaluated in polypropylene-copolymer and in base fuel.

The analytical and spectroscopic methods such as elemental analysis, IR, ^{1}H NMR, CMR and Mass spectral data have been utilised in establishing the structure of the compounds synthesised during the course of this work.

The thesis is divided into five chapters.

Chapter 1 : *Introduction*

This chapter deals with general introduction to antioxidants, classification, and types of combinations, mechanism of action, applications and role of antioxidants in biological systems.

Chapter 2

Section 1 : Synthesis and Characterisation of Antioxidants based on Hindered phenol and Hindered amines.

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. However their uses are generally limited to the applications in which their discolouring characteristic can be tolerated or masked. In order to overcome the above mentioned drawbacks of hindered phenols and hindered amines it was thought worthwhile to synthesise compounds with both the stabilising moieties present together in the same molecule. Therefore antioxidants based on hindered phenol in combination with hindered amines were synthesised.

In this section we discuss the synthesis, characterisation and activity evaluation of some new antioxidants based on hindered phenol and hindered amines. In order to introduce aminomethyl group at the position para to hydroxyl group in 2,6-di-tert-

butyl-4-methylphenol (BHT), 2,6-di-tert-butyl-4-chloromethyl phenol was synthesised starting from 2,6-di-tert-butylphenol by the application of chloromethylation. Structure of 2,6-di-tert-butyl-4-chloromethyl phenol was established by converting the chloromethyl group into aldehydic group by the application of Sommlet reaction. Same aldehyde was also synthesised by a reported method and compared. Chloromethyl derivative on reaction with various primary and secondary amines afforded aminomethyl linkage at the position para to hydroxy group in BHT. The amino methyl linkage was also introduced by the application of Mannich reaction on 2,6-di-tert-butyl phenol by using secondary amine in the presence of formalin. Some of the synthesised antioxidants were tested for antioxidant activity in base fuel (MS) and base fuel (FCC gasoline) by potential residue method at Indian Oil Corporation Limited. The activity of the synthesised antioxidant was found to be comparable with the commercial sample (UOP-5).

Section 2 : Synthesis of Antioxidants by the application of Wittig reaction

In this section we discuss the synthesis and characterisation of some new antioxidants based on hindered phenol by the application of Wittig reaction. As a prelude to the present work, prior work in this field has been reviewed here. From the literature survey it is revealed that powerful synergism is achieved by using combination of hindered phenol and phosphite or phosphonites. Among the antioxidants based on hindered phenol, the use of combination of hindered phenol with phosphite is less extensively studied, whereas the combination of hindered phenol with phosphine is apparently not reported. With this in view, 3,5-di-tert-butyl-4-hydroxybenzyl triphenyl phosphonium chloride, a Wittig salt was synthesised by the reaction of 2,6-di-tert-butyl-4-chloromethyl phenol with triphenyl phosphine. The activity evaluation of this compound in polypropylene-copolymer is discussed in chapter 5. The ethylenic linkage was introduced at the

position para to hydroxy group in BHT by reaction of Wittig salt with various substituted aromatic aldehydes and ketone.

Chapter 3 : *Antioxidants based on Hindered Phenol and Oxygen heterocyclics bridged by Chalcone, Pyrazoline and Phenyl pyrazoline.*

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 scavenger. During the course of this work biologically active antioxidants based on hindered phenol and oxygen heterocyclics bridged by chalcone, pyrazoline and phenyl pyrazoline have been synthesised. This synthesis was achieved by converting the methyl group in BHT into an aldehydic group by using a known method. The aldehyde on reaction with phenolic ketones in acidic medium (Claisen-Schmidt condensation) afforded chalcone linkage. These chalcones on cyclocondensation with hydrazine hydrate and phenyl hydrazine yielded 2-pyrazoline and 1-phenyl-2-pyrazoline derivatives respectively. Some of the *o*-hydroxy chalcones on reaction with mineral acid gave flavanone. 3,5-Di-tert-butyl-4-hydroxybenzaldehyde on reaction with ethylaceto-acetate and urea afforded dihydropyrimidine moiety at the position para to hydroxy group in BHT.

The screening for antibacterial activity of the synthesised compounds against bacteria *E. Coli, S.Aureus, S.Typhi, P.Vulgari and S.Dysenteriae* has been carried out by using Bore-well method. In these experiments, BHT was taken as a reference standard. Most of the compounds showed encouraging antibacterial activity; some of the compounds were found to be more active than BHT. By modifying the structure of BHT, compounds having better biological significance could be obtained.

Chapter 4

Section 1 : Synthesis and Characterisation of Irganox 1076 homologue – A novel observation.

Octadecyl-3-(3',5'-di-tert-butyl-4'-hydroxyphenyl) propanoate commonly known as Irganox 1076 and its derivatives are widely used as antioxidants in polymer and in foods. It is well established that the increase in the chain length at the position para to hydroxy group in 2,6-di-tert-butyl-4-methylphenol would enhance the antioxidant activity. The present work deals with the synthesis of homologue of Irganox – 1076 by increasing the chain length by one carbon atom. 2,6-Di-tert-butyl phenol on reaction with succinic anhydride in the presence of Lewis acid leads to migration and de-tert-butylation without tert-butyl acceptor along with *O*- and *C*-succinolyated products. Desirable product 3-(3',5'-di-tert-butyl-4'-hydroxybenzoyl) propanoic acid is obtained along with small amount of 4-tert-butyl phenol when nitrobenzene was used as solvent. The use of carbon disulphide as solvent afforded 3-(4'-tert-butylcarbphenoxy) propanoic acid. 3-(3',5'-Di-tert-butyl-4'-hydroxybenzoyl) propanoic acid on reduction with zinc amalgam (Clemmenson reduction) yielded 3-(3',5'-di-tert-butyl-4'-hydroxy phenyl) butanoic acid. The butanoic acid derivative on esterification with appropriate alcohol furnished homologue of Irganox-1076. The work was extended by replacing octadecyl group by ethyl, n-propyl, iso-propyl and iso-amyl groups.

Section 2 : Preparation and Reactions of 1-(3',5'-di-tert-butyl-4'-hydroxy phenyl)-2-bromoethanone.

In more demanding long-term heat exposure, the choice is always in favour of high molecular weight antioxidants, which may ensure lower volatility. Present work deals with structure modification of BHT by introducing various high molecular weight functionalities at the para position of hydroxy group. In this section synthesis and reactions of 1-(3',5'-di-tert-butyl-4'-hydroxyphenyl)-2-

bromoethanone is discussed. 3,5-Di-tert-butyl-4-hydroxyacetophenone on treatment with liquid bromine yielded 1-(3',5'-di-tert-butyl-4'-hydroxyphenyl)-2-bromoethanone and 1-(3',5'-di-tert-butyl-4'-hydroxyphenyl)-2,2-dibromo ethanone. Bromoethanone derivative on treatment with different substituted phenols gave 2-phenoxy ethanone derivatives, which on cyclisation with thiourea (Hantzsch synthesis) afforded 2-aminothiazole moiety para to hydroxyl group in BHT and on reaction with *o*-hydroxybenzaldehyde in the presence of basic catalyst afforded 2-(3',5'-di-tert-butyl-4'-hydroxybenzoyl) benzofuran. 1-(3',5'-Di-tert-butyl-4'-hydroxyphenyl)-2-(4'-methyl phenoxy)ethanone was tested in polypropylene-copolymer and the activity was found to be comparable with that of BHT.

Chapter 5 *: Hindered phenols as Stabilisers for Polypropylene-copolymer(PPCP)*

In this chapter we discuss the activity evaluation of synthesised and commercial antioxidants on unstablised PPCP. Melt mixing, multiple extrusion, melt flow rate and oxidative induction time techniques are employed for the activity evaluation. Polypropylene-copolymer grade MI 3530 having melt flow rate 4.3g/10min was used for all the experiments. Synthesised antioxidants showed potent antioxidant activity in PPCP. The following antioxidants were selected for the study.

1) 3,5-di-tert-butyl-4-hydroxylbenzyl triphenyl phosphonium chloride **(AO1)**
2) 4-(3',5'-di-tert-butyl-4'-hydroxyphenyl)-5-carbethoxy-6-methyl pyrimidin-2-one **(AO2)**
3) 1-(3',5'-di-tert-butyl-4'-hydroxyphenyl)-2-(4'-methylphenoxy) ethanone **(AO3)**
4) N-(4'-ethylphenyl)-3,5-di-tert-butyl-4-hydroxy benzylamine **(AO4)**
5) 1-(3',5'-di-tert-butyl-4'-hydroxybenzyl)-4- phenyl piperazine **(AO5)** and
6) 1-(3',5'-di-tert-butyl-4'-hydroxybenzyl) piperidine **(AO6)**

This study is divided in to two parts depending upon the chemical structure of the synthesised antioxidants.

In part 1 antioxidants AO1, AO2, AO3 and BHT were considered and degree of stabilisation was found to be as follows

AO2>AO1>BHT~AO3.

In part 2 antioxidants AO4, AO5, AO6 and BHT were selected for activity evaluation. The stabilisation efficiency of these antioxidants was found to be in the following order

AO5>AO4>AO6>BHT.

Conclusion

Antioxidants based on hindered phenol in combination with hindered amines afforded the antioxidants with effective antioxidant activity in base fuel. The antioxidants with same combination also enhanced the thermal stability of polypropylene-copolymer. Antioxidants based on hindered phenol and oxygen heterocyclics bridged by chalcone, pyrazoline and phenyl pyrazoline showed encouraging antibacterial activity. Increase in molecular weight could decrease the volatility of the antioxidant. Due to this the loss of antioxidants from the surface of the material was reduced and as a result, better performance maxima was obtained. Various synergistic combinations greatly influenced the performance of antioxidants. From the results of present study it is evident that the stabilisation efficiency of synthesised antioxidant is encouraging and hence desirable.