CHAPTER 1

INTRODUCTION

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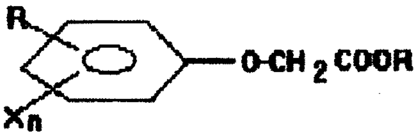
1.1 Chlorine Substituted and other phenoxy Alkanoic acids as Herbicides :-

Phenoxy acetic acid derivatives like 2,4-D have been identified as plant growth regulators and herbicides, and are widely used for control of weeds in cereal crops, grass plastures, lawns etc. 2-Phenoxypropionic as well as 4-phenoxybutyric acids are preferred because of their low or negligible toxicity to crops or plants.

Importance of Phenoxy Alkanoic Acid And Derevatives

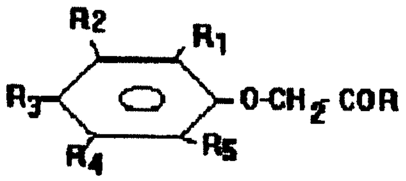
Since the World War II, various Phenoxy acetic acid derivatives as selective herbicides for crop plants, were prepared.[1]. 4-Isopropylphenoxyacetic acid (100 ppm) totally controlled Echinochloa crus galli without phytotoxic effects on rice, Japanese white radish, Lettuce, tomato and cucumber.

Phenoxyacetate compounds as plant growth regulators were synthesized[2]. which contain phenoxyacetates



(R=Me, Et, Isopropyl or tert. butyl and x = halo n=0-2), their salts or esters, with exception of 3-tert. butyl Phenoxy acetic acid and 4-tert. butyl Phenoxy acetic acid. Thus 3-isopropyl Phenoxy acedic acid 10 mg in 2 ml acetone and 6 ml 10 ppm sorbol w-150 and water 20 ml to form a solution at 500 ppm increased cucumber growth by 185%. Plant growth regulating activity of brominated 3 or 4 substituted lower alkyl phenols and phenoxy acetic acid were also studied[3]. Sixteen 3-or 4- alkyl (Me, Et, Isopro and tert. but.) Phenols (I) and thirteen 3 or 4 alkyl phenoxy acetic acids (II) and 3 or 4 tert. butyl phenoxy α-propionic acids were brominated. In germination tests with oryza sativa Raphanus sativa and Lactuca sativa with 0.1 to 100ppm of 12 I and 12 II derivatives, such as those 3 Et-4,6-dibromo and 3-Isopropyl 4,6-dibromo phenols showed stronger inhibitory activity to rice at 100 ppm than that of 2,4,D.

Synthesis and biologial activity of [(3-pentadecylaryl) oxy] acetic acids, their hydrazides and cyclic derivatives, oxadiazole and pyrroles were determined[4]. Phenoxy acetic acids III exhibited antiinflammatory activity. Phenol & $Cl-CH_2-COOH$ gave III (R-OH) which was converted into IV and V by appropriate reactions.



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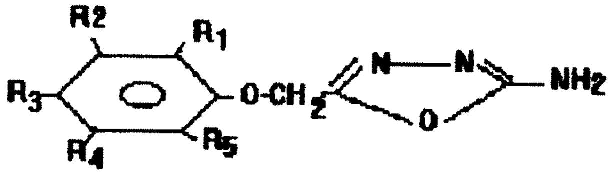

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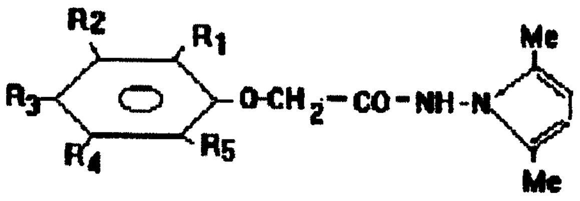


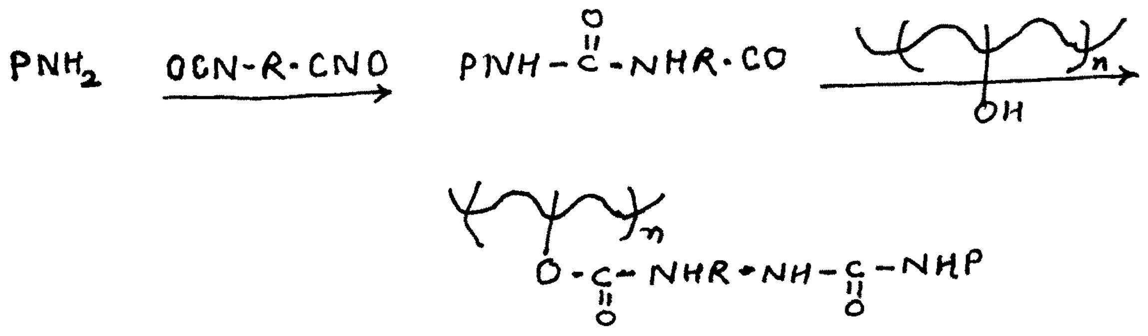
(V)

Herbicides linked to polymers have been in use and Table I shows some of the herbicide polymer combinations.

Table I Herbicide polymer combinations

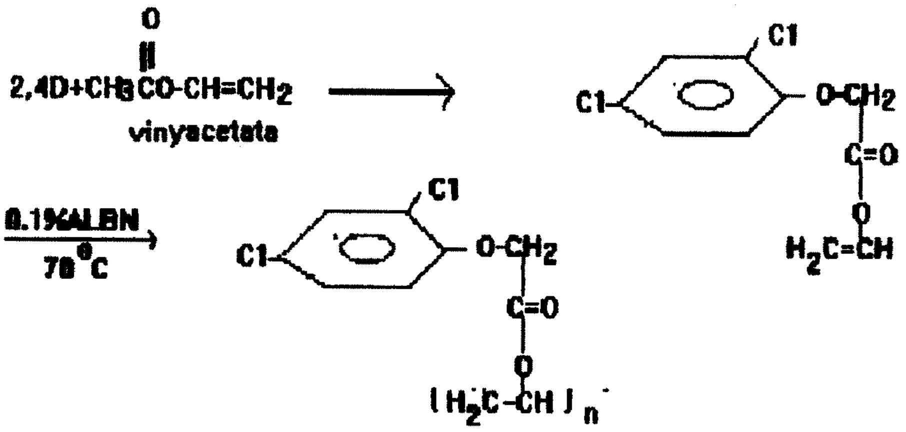
Sr. No.	Herbicide	Polymers
1	2,4-D	Cellulose, bark kraft lignin Polyvinylalcohol.
2	2,4,5,T	Cellulose, bark, lignin
3	2(2,4,5-Trichloro Phenoxy) propionic acid (Silvex)	Bark, Kraft, lignin
4	4(4-chloro-2-methyl Phenoxy)butyric acid	Bark, Kraft, lignin
5	4(2,4,dichlorophenoxy) butyric acid(2,4,DB)	Kraft, lignin, Bark
6	4(2,4,5 trichloro phenoxy)butyric acid (2,4,5 TB)	Bark, Kraft, Lignin

Active ingredients and polymers were linked by using multifunctional entity as shown below



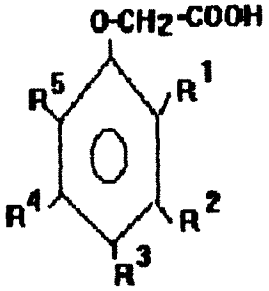
Both natural and synthetic polymers can be used as support to link the active ingredients which were released due to chemical or biological degradation of the covalent bond.

In another method[5], the active agent was chemically linked to monomer and then it was polymerized.



Polymers of this type were developed by Harris and Coworkers[6], using 2,4,D or 2,4,5,T (Silvex) herbicides as pendant chains. Reaction of these herbicides was carried out with the alcohol residues of the desired acrylic esters. eg. 2,4,D with acrylic ester gave 2 acryloyloxyethyl-2,4-dichloro phenoxyacetate (2A2,4,D). Polymerization of this derivative was then initiated by free radical under mild conditions. Copolymerization also can be effected. Thus by copolymerizing 2A2,4-D with vinyl monomers containing hydrophilic residue such as trimethylamine methacrylamide (TAM) hydrophilic TAM residue were included in the polymer back bone. These pendant chain systems offer an important advantage over other release systems in agricultural applications on economic considerations and can be detected quantitatively by UV and IR spectroscopically.

Aryloxy acetic acid of general formula



were prepared, where in R^1 to R^5 can be same or different substituents. Na, K or Li salts of these acids in alcoholic solution with alcoholic metallic hydroxides or alcoholate were prepared[7]. Solubility of caffine or 8-methyl caffine in the solution of alkali salts of above alkanoic acids was determined. Phenoxy alkanoic acids having substituents with +I and +M effect had higher dissolution power than unsubstituted $PhO-CH_2-COOH$. This property was used in surfactants. Nitrophenoxy acetamides and 2,4, dihydroxy-5-nitro-propiophenone derivatives were prepared and found to be having insecticidal action[8]. Benzyloxy and phenoxy acids with different substituents on the benzene ring were synthesized and they were tested for potential antisicking agents and activity relationship. A large number of different compound were synthesized and evaluated in vitro for antigelling activity when 2-(-p-bromophenoxy)ethyl malonic acid was found to be most active compound.[9]

The phenoxy alkanoic acids have greater herbicidal activity, specially for dicotyledone weed species. The derivatives of some of the phenoxyacetic acids are used in antichlolingerics, hypoglycermics & diurethics[10]. Few phenoxyacetic acids are reported to be good fungicides. Phenoxyalkanoic acids are good herbicides and are easily biodegradable. Their degradation mechanism is reported in the literature[11]. These do not pollute the environment and are not hazardous to use. So they can be handled safely. 2,4,D acetamide and diethylamine derivative of 2,4,D have been reported for the control of water hyacinth.

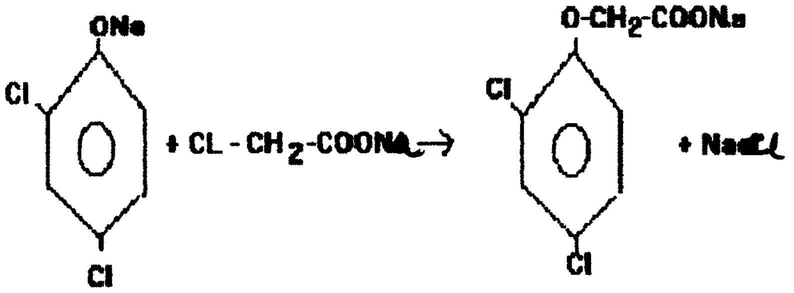
In the chemical control of water hyacinth it was observed that the complete destruction of water hyacinth take place in 10 weeks by spraying CIDICO, a product of N.V.Amster damsche, chinernifabrik-Holland containing 80-82% of sodium salt of 2,4,D. Similarly water hyacinth could be killed by spraying methoxane (2 methyl-4-chloro phenoxy acetic acid)[13], repeatedly in 15 days.

1.2 Synthesis and Methods of preparations of phenoxy Alkanoic acids :-

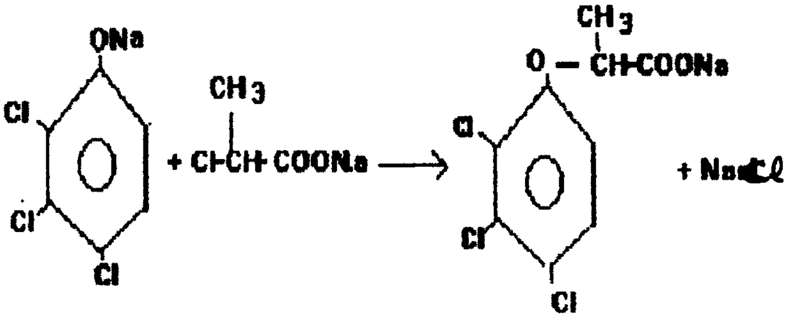
Synthesis of Phenoxyalkanoic acids

The usual method for synthesis of phenoxyacetic acid and 2 phenoxy propionic acid herbicides involved the reaction of corresponding phenols with appropriate chloroalkanoic acids in alkaline medium (pH 10-12) at about 100°C[14].

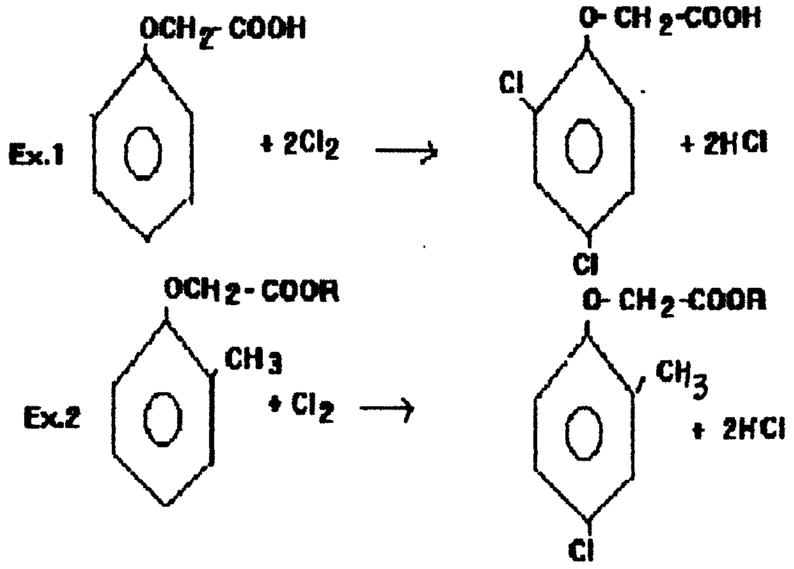
ex.1



ex.2



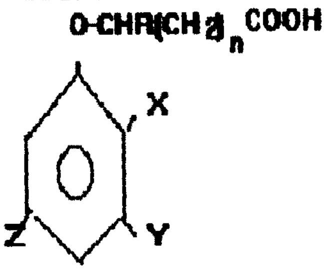
The chlorophenoxy alkanoic acids or their esters are prepared by chlorinating corresponding acids or esters[15,16].



Some of the widely used herbicides based on phenoxy alkanoic acids are shown in Table II.

Table II List of Phenoxyalkanoic acid Herbicides

Basic Structure



Sr. No	Name	R	X	Y	Z	n
1)	2,4 dichlorophenoxy acetic acid 2,4D	H	Cl	Cl	H	0
2)	4-(2,4 dichlorophenoxy) butyric acid (2,4 DB)	H	Cl	Cl	H	2
3)	(2,4,5-Trichlorophenoxy) acetic acid (2,4,5-T)	H	Cl	Cl	Cl	0
4)	4(2,4,5-Trichlorophenoxy butyric acid(2,4,5-TB)	H	Cl	Cl	Cl	2
5)	[(4-chloro-O-Tolyl-oxy)] acetic acid (MCPA)	H	CH_3	Cl	H	0
6)	2-(2,4,5-Trichlorophenoxy) propionic acid (Silvex)	H	CH_3	Cl	H	0

Methods of preparations of Phenoxy alkanoic acids[17]

The α-aryloxyalkanoic acids used for various purposes were prepared by four methods.

Method A :- To a solution of 0.4 mole phenol 0.2 mole of an α-haloalkanoic acid in 90 ml ethanol was added on ice cooled solution of 0.5 mole Sodium hydroxide in 30 ml water, the mixture refluxed 22 hours, the ethanol distilled in vacuo and the residue dissolved in 200 ml water and acidified to pH 2. The precipitated acid was dissolved in ether, extracted with 5% sodium bicarbonate solution and the aqueous extract acidified to give the free acid.

Method B :- A solution of 0.5 mole of α-haloacid and 0.5 mole of sodium hydroxide in 125 ml water was mixed with a solution of 0.5 mole sodium phenoxide. The mixture heated on a steam bath for 20 hours and acidified and the oily precipitate dissolved in ether. The ether solution was extracted with 5% sodium bicarbonate solution which yielded the acid on acidification.

Method C :- In a flask fitted with a stirrer, reflux condenser above a Dean Stark water trap and a dropping funnel, 0.2 mole of phenol,250 ml Toluene and 0.25 mole sodium hydroxide was refluxed untill 3.3 ml of water had collected in the trap. After a dropwise addition of 0.25 mole Ethyl α-haloalkanoate, the mixture was refluxed overnight. The ester saponified with 40 ml methanol 0.3 mole sodium hydroxide and 50 ml water and the mixture worked up to yield the acid.

Method D :- A solution of 0.156 mole sodium, 0.156 mole Ethyl α haloalkanoate and 0.156 mole phenol in 120 ml absolute ethanol was refluxed 4 hours and the ester saponified by adding 120 ml 2N sodium hydroxide and refluxing the mixture 1 hour worked up the yielded acid.

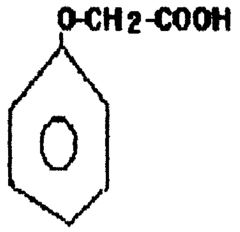
Recently using a modified procedure aryloxy acetic acids[18] were prepared using solid liquid phase transfer catalyst, by stirring R-OH (R=ph, α-β-naphthyl, 4 MeO. C_6H_4, 2-3-4 $Me_3(C_6H_4$, $2ClC_6H_4$) with $Cl-CH_2-COOH$, NaoH and PEG 400 in MeCN at 125°C for 3 hours. Yield obtained of $R-O-CH_2-COOH$ were 38-90%. Alkyl phenoxy alkanoic acids could be purified if desired[19] by separation techniques such as adsorption, partition , TLC and reverse phase HPTLC.

2-Chloro-6-methyl phenoxy and (4-Cl,2-Me phenoxy) alkanoic acids[20] were prepared by the chlorination of 6-Me-phenoxy and 2-methyl phenoxy alkanoic acids. By utilising exchage resins as catayst $R-O-CH_2-COOR^1$ ($R = Ph, O-NO_2-C_6H_4$, $P-NO_2-C_6H_4$, ß-naphthyl, $R^1=Et$) were prepared[21] in 80-92% yield by the reaction of Amberlite IRA 400 bound R-OH with $Cl-CH_2-COOEt$ in EtOH. Using MeOH transesterification occured after 18 hours. 2-methyl -4- chlorophenoxyacetic acid was prepared[22] as a herbicide by Demovic Stanislav, from 2 methyl phenoxy acetic acid and or its sodium salt by chlorination and final treatment with NaClO. Using anion exchange resins aryloxy acetic acids and their nitro substituted derivatives were synthesized, in better yields. Phenoxides supported on Amberlite IRA 400 on reaction with $Cl-CH_2-COONa$ give aryloxy acetic acid in 96-99% yields. Nitrophenols, 4-hydrory coumarins and $P-HO-C_6H_4-COOEt$ gave excellent yields of the products[23]. Synthesis of some substituted phenoxy alkyl carboxylic acids and their properties as growth substances were studied. The method involved reaction of sodium derivative of phenol in absolute ethanol with the ethyl ester of an α bromo acid, saponification of resultant ester, acidification and recrystallisation and gave almost quantitative yields of required acids. Details for the preparation of 2,4 dichlorophenoxy acetic acid in 95% yield are reported[24]. α-phenoxy butyric acid and x-phenoxy proplonic acids were also prepared in the similar way. O-Chloro, m-Chloro α phenoxy propionic and butyric acid were prepared. The solubility of most of these acids in water was studied. A new method of testing compounds on young tomato plants for physiological response as growth substances was developed. Halogens or methyl group were found to be most important in effecting activity for cell elongation. In phenoxy alkyl carboxylic acids, halogens were more effective than methyl group at 2,4,6 position in the ring those in which substituent exert influence. It has been observed that the phenoxy acetic acid is stronger then the parent acid and undergoes reactions of alkylcarboxylic acids. The phenoxyalkanoic acids are sparingly soluble in water but their esters are oil soluble and thus in combination with suitable emulsifying agent, they are used in herbicidal formulation. The ester formation is an important factor in the manufacture of many phenoxyalkanoic acids herbicidal formulations as their esters exhibit greater herbicidal activity than the parent acids because of their improved absorption by the target plants.

The esters of low molecular weight alcohols of phenoxyalkanoic acids are volatile and may cause hazards to non-target crops but low volatile esters are safer. Tetrahydrofurfuryl, butoxyethyl, iso-octyl or 2-ethylhexyl derivatives of phenoxyalkanoic acids are some of the low volatile esters.

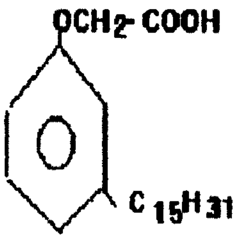
1.3 CNSL and it's Utilization

As Cashewnut shell liquid and its derivatives viz cardanol tetrahydroanacardol etc are less volatile due to long alkyl ($C_{15}H_{31}$) substituent meta to phenolic hyroxyl group, it is expected that the esters derived from novel (3-pentadecyl) phenoxyalkanoic acid will be nonvolatile and safer to use, than corresponding nonsubstituted penoxyalkanoic acid esters. Even the esters derived from the low molecular weight alcohols are anticipated to be nonvolatile due to increased molecular weights in CNSL derived products, for example Phenol (mol.wt94, bp $184^{\circ}C$; cashewphenol i.e. cardanol (mol. wt. 304) bp $220^{\circ}C$/ 5mm Hg.



Mol. wt. 188

Phenoxyacetic acid



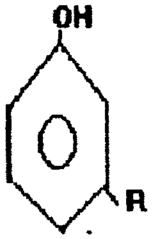
Mol. wt. 362.

(3-pentadecyl) phenoxyacetic acid.

Cashewnut Shell Liquid (CNSL) :- Cashewnut shell liquid (CNSL) is an important byproduct obtained in the isolation of Kernals from Cashewnuts. It is viscous resinous agricultural byproduct, and is a source of phenol with a unsaturated carbon chain at meta position.

Harvey and Caplon distilled the commercial CNSL under vaccum and 70% of the total distillate was found to be single phenolic compound with an unsaturated side chain at meta position. This substance was named as cardanol, or 3 pentadeceneyl phenol[25]

Dowson and Coworkers[26] have studied the chemistry of cardanol in detail and established following structure.



$R = C_{15}H_{27}$
$C_{15}H_{29}$
$C_{15}H_{31}$

Specification and applications of cardanol are given in Table III. It is structurally similar to m-cresol and behaves as a phenol. This structural feature was utilized for various commercial applications in the field of polymers and agriculture. The products obtained from cardanol have many advantages over those manufactured from other substituted phenols. It is therefore widely used in the manufacture of surface coatings, Insulating Varnishes, Oil and Alcohol soluble resins, Laminating resins, Rubber compounding, Azo dyes etc.

The components of commercial cardanol differs in the degree of unsaturation of the side chain but for all practical purposes it can be represented by the following formula.

$C_6H_4(OH)-(CH_2)_7-CH=CH-CH_2-CH=CH-(CH_2)_2-CH_3$

The average unsaturation of about two double bonds in the side chain of the cardanol molecules makes cross linking easy and give a satisfactory gradual drying and baking properties to paints prepared from it. Because of it's pecular structure cardanol varnishes have high electric insulation, greater resistance to water, chemicals and also good flexibility. The long hydrocarbon side chain imparts to cardanol aldehyde condensate greater solubility in drying oils such as linseed DCO or tung oil and aliphatic hydrocarbons.

Table III

	Grade-I	Special Grade
1) Structural Formula	$HO-C_6H_4-C_{15}H_{27}$	$HO-C_6H_4C_{15}H_{27}$
2) Density	0.9272-0.935	0.9272-0.935
3) Viscosity at 30°C	55.65(cp)	52.58(cp)
4) Volatiles maximum as per IS101-1964	3%	3%
5) Ash contents	Negligible	Negligible
6) Iodine value IS840 -1964(catalytic method)	Min 301	Min 325
7) Acid value	Max 5	Max 5
8) Hydroxyl value	180-190	180-190
9) Colour gardener (Freshly distilled)	(Dark Brown)	(Pale Straw)

Following are some of the suggested applications of cardanol.

1. Oil Soluble Resins :- The long meta substituted hydro carbon chain of cardanol imparts to resins prepared from it easy solubility in drying oils and superior electrical insulation and resistance to water and chemicals. Both solid and semisolid type resol or novolac resins could be manufactured from cardanol depending upon the nature of the catalyst and aldehyde used.

2. Electrical Insulating and Impregnating Varnishes :- Cardanol resin varnishes have good electrical insulating properties and resistance against water and chemicals. They give superior quality stamping varnishes. Because of their high insulation and low dielectric losses, these varnishes are preferred to compositions based on usual phenol such as

cresol or substituted phenols.

3. <u>Surface coatings and Paints</u> :- Cardanol resin varnishes in addition to water and chemical resistance have good air drying and baking properties. These compositions are suitable for wood finishes, food can lacquers, textile bobbins and high quality paints. Stoving paints can be prepared which could be baked at 60°C. The cardanol based resins have good compatability with ohter synthetic resins such as alkyds, epoxies , chlorinated rubber, phenolic etc and can serve as a raw material for variety of paints.

4. <u>Lamination Industry</u> :- By partly replacing the phenol or cresol in the alcohol soluble resins used for lamination one could prepare resins which imparts greater flexibility resistance to chemical and superior electrical insulation to the lamination sheets.

5. <u>Surface active agents</u> :- Sulphonated ether of cardanol has been found to be excellent wetting agent and finds use in textile industry. Ethoxylated tetrahydrocardanol sulphonate performs better at high temperature than the detergents based on dodocyl benzene.

6 <u>Pesticides</u> :- Chlorinated cardanol is reported to have insecticidal, pesticidal and germicidal properties. Cardanol formaldehyde resin is also used as a solvent for well known pesticides such as pyrethrin and rotanes. p-nitro tetrahydro cardanol finds use as a coupling compound in sprayable pesticides such as parathion.

7 <u>Rubber compoundings</u> :- Oil soluble cardanol resins are used in rubber compounding. They impart high tear strenght and

resistance against petroleum based solvents. Pure cardanol acts as a deoxident and plastisizer when incorporated in rubber. Its ethers are also used as plasticizers for synthetic rubber to reduce the shore hardness and improve the ageing properties.

8 Azo dyes :- 3-pentadecyl phenol and sulphonated products of cardanol are being used as intermediates for Azo Dyes.

9 Wax substitutes :- Waxing solids with high melting points could be prepared from cardanol resins and suitable amide such as stearamide. When 3-pentadecyl phenol is reacted with 1:4 dichlorobutane a wax with a melting point of 90/93°C is obtained. These waxes are comparatively cheaper and compatible with other waxes such as bees wax, carnaba wax paraffin wax etc.

10. Mineral oil additives :- Mineral oil additives based on amino cardanol, ethers of hydrogenated cardanol and salts of its sulphonated ethers are found to improve the viscosity index of mineral oil, inhibit sludge formation and antioxident properties.

11. Adhesives :- Adhesives and acid resistance cements can be prepared from cardanol or its derivatives. These have good adhesion to metal as well as cement surfaces.

12. Food can Lacquers :- Excellent food can lacquers could be prepared by reacting cardanol resins with vinyl monomers. These lacquers give golden yellow films, which would be air drying or baking.

13. Brakelinings and Clutch facings :- An excellent quality of friction dust could be prepared from cardanol which finds

use in brakelinings and clutch facings.

Ghatge and Patil have synthesised 3-pentadeceny/phenoxy acetic acid for use as coating composition.[27]

Ghatge and Amarnath[28] have studied the herbicidal activity of 2-butoxy ethanol ester of 2,4-dichloro-5-pentadecyl phenoxy acetic acid against water hyacinth in composition with 2-butoxy ethanol ester of 2,4-D. However recent environmental concerns prefers avoidance of chlorination of phenolic moieties so as to avoid PCB formation. Since Cashewnut shell liquid is vesicant and corrosive material and its derivatives have been utilised for the manufacture of mosquito larvicides[29] detergent[30], it is logical to assign potential herbicidal activity to parent CNSL, cardanol, tetrahydroanacardol (THA) or Phenoxy acetic acid derivatives based on THA.

In view of this, it was proposed to synthesize a series of new alkyl esters of CNSL derived 3-pentadecyl phenoxy acetic acid, and to perform complete characterisation of all the esters by spectroscopic UV, IR, NMR -(PMR & CMR). These esters may have potential herbicidal activity, which is inherent to CNSL derivatives, even in the absence of chloro-derivatives.

Similarly a series of aromatic amide derivatives of (3-pentadecyl) phenoxy acetic acid was synthesized by direct amidation of acid with various ring substituted aromatic primary amines using triphenyl phosphite and lithium chloride Catalyst in NMP solvent. Each of the amide product have been characterised in detail by spectroscopic procedures to assign the structural moieties.