2. LITERATURE REVIEW:

2.1 8-hydroxyquinoline and its derivatives:

8-Hydroxyquinoline (8-quinolinol, oxine) might be thought to function as a phenol, but of the 7 isomeric Hydroxyquinolines only oxine exhibits significant antimicrobial activity, and is the only one to have the capacity to chelate metals. If the hydroxyl group is blocked so that the compound is unable to chelate, as in the methyl ether, the antimicrobial activity is destroyed. The relationship between chelation and activity of oxine has been investigated. Oxine itself is inactive, and exerts activity by virtue of the metal chelates produced in its reaction with metal ions in the medium. Used by itself or as the sulphate (Chinosol) or benzoate in antiseptics, the effect is bacteriostatic and fungistatic rather than microbiocidal. Inhibitory action is more pronounced upon gram-positive than gram-negative bacteria; the growth-preventing concentrations for staphylococci being 10 ppm; for streptococci 20 ppm; for Salmonella typhosa and for E. coli 100 ppm. However, a 1% solution requires at least 10 hours to kill staphylococci and 30 hours for E. coli bacilli. The oxine benzoate was the most active antifungal agent in a series of 24 derivatives of quinoline tested. A 2.5% solution of this compound was successful in treating dermatophytosis [13]. Iron and cupric salts were found to prolong the antibacterial effect of oxine on teeth. 6-carbethoxy-3-aryl-5-(2'-chloro-6',8'-dimethylquinolin-3'-yl)-2-cyclohexenones known quinoline derivatives found to be associated with various pharmacological activities such as antifungal, antibacterial, anticoagulant, antipyretic, anti-inflammatory etc reported by Nimavat et.all [14]

Certain halogen derivatives of 8-hydroxyquinoline have a record of therapeutic efficacy in the treatment of cutaneous fungus infections and also of amebic dysentery. Among these are 5-chloro-7-iodo-8-quinolinol(iodochlorhydroxyquin,Vioform), 5,7-diiodo-8-hydroxyquinoline(diiodohydroxyquin), and sodium 7-iodo-8-hydroxyquinoline-5-sulfonate (chinofoin)[15]. Copper oxinate the copper compound of 8-hydroxyquinoline, is employed as an industrial preservative for a variety of purposes, including the protection of wood and textiles against fungus-caused rotting, and interior paints for food plants. It has 25 times greater antifungal activity than oxine [16].
The antibacterial activity of 8-hydroxyquinoline and its derivatives is long-known. The drugs from this group are used as chemotherapeutics in medicine for more than 120 years [17, 18, 19, 20], and in analytical chemistry as chelators [21, 22].

Some newly synthesized derivatives of 8-Quinolinol were shown to exhibit a higher microbiological activity [23, 24, 25].

8-Hydroxyquinoline (8-HQ) moiety has received continuous attention as a platform for the construction of a number of selective and efficient ionophores.[26] The most interesting feature of 8-HQ is its very low quantum yield in aqueous or organic solutions but the fluorescence enhancement occurred from cation binding and many metal chelates of 8-HQ exhibit intense fluorescences.[27,28] Although the selectivity of 8-HQ and its simple derivative is rather poor, it can be improved by appropriate substitution on the phenolic oxygen atom or aromatic rings.[29]
2.2 Reviews about 5-chloromethyl-8-hydroxy quinoline:

The survey of literature reveals that 5-chloromethyl-8-hydroxy quinoline (CMQ) is a versatile derivative of 8-hydroxyquinoline. It can be easily prepared by the room temperature reaction of 8-hydroxy quinoline. Paraformaldehyde, con.HCl and dry HCl gas [30]. It is stable in form of hydrochloride otherwise it hydrolyzes to methyl group.

The reports [30] included the number of derivative of CMQ by the reaction of CMQ with alcohols and secondary amines. Aristov. et. al. have documented several reports about number of 5-substituted derivatives from CMQ having the structures as follows.

\[ R = \text{Alkyl, Cycloalkyl, Benzyl} \]

The derivatives were monitored for anthelmintics, rematacides and fungicides [31].

The coumarin ring containing derivatives has also been reported from CMQ hydroxy coumarin.
The dental plaque inhibitors from CMQ derivatives were prepared by Victor et al. [32]

H-Juerjea and Roth Hermann reported [33] that reaction between CMQ and urea/guanidine afforded the represented

N,N'-bis(8-hydroxyquinolin-5-yl methyl) urea

1,3-N,N'-bis(8-hydroxyquinolin-5-yl methyl) guanidine

The fungicidal compound has been prepared having following formula [34].

D. Pennelolce reported the corbostyriss derivatives containing 8-hydroxy quinoline [35]. The tetrakis 8-hydroxy quinoline methyl ethylene alkyl diamine shown below has been prepared for their complexation [36,37]. Similarly the glycine ester from CMQ has also been reported [38].
The patent has been reported about the 5-methylpiperazinyl derivatives for Fschamia treatment [39].

Some reports about the metal analysis complexation and electroanalysis of these derivatives are also found. [37]

As CMQ having reactive group, number of ion-exchange resins has been prepared by reaction of CMQ with active reactive group of polymers [40, 41].

The cellulose is a high molecular weight natural polymer and its reaction with CMQ affords the 8-Hydroxy quinoline-cellulose product which is applied as good ion-exchanger [42].

The well-known polymer say polystyrene and or styrene divinyl benzene copolymer were aminated and these on treatment with CMQ afford good ion-exchangers.

Polyethylene amine, polyethylene polyamine and polyxylene polyamines reacted with CMQ. The authors suggested that these products are good metal chelating agents.

Ulkelov et.al. reported the ion-exchange resin by condensation of CMQ and poly thiocyanatoaniline.

Taken et.al. reported [43] the important aspect about florescent chelate based on reaction product of CMQ and water soluble polymers.

W.R.David suggested that polymers of olefin bearing bidentate ligands are useful as protective coating and primers. Thus he prepared such polymer by reaction between poly (2-hydroxy-ethylmethacrylate) and CMQ.
The chelate resin patented as reaction product between CMQ and acrylonitrile-divinyl benzene-ethylene diamine copolymer.

8-hydroxy quinoline terminated polyether was prepared by the reaction between amino terminated polyether and CMQ [44, 45].

The various scientists [46-49] have reported the bis-8-hydroxy quinoline prepared from CMQ and their co-ordination polymers as per below given structure.

Some of the ions exchanging resins are also with good potentiality. I.M.Vohra, synthesized compounds for his P.HD work, by reaction of CMQ with heterocyclic derivatives recently [50].

N. Manolova et all, synthesized Polyethers with 8-hydroxy-5-quinolinyl end-groups (P–Q) by reaction of polyethers having amino end-groups with 5-chloromethyl-8-quinolinol hydrochloride[51].

Bis (bidentate) ligand, namely 5, 5′- (2, 2′- (phenyl azanediyl) bis (ethane-2, 1 -diyl) bis (oxy) bis (methylene) diquinolin –8 - ol) (PBEQ), by condensation of 5 – chloromethyl –8 - hydroxyquinoline hydrochloride with N, N – Di (2 - hydroxy ethyl) aniline in the presence of a base catalyst, synthesized by Khyati Patel et al[52].

Aradhana verma et all. Synthesized 5-((1-(2-methyl-5-nitro-1H-imidazol-1-yl) propan-2-yloxy) methyl)quinolin-8-ol. (Formation of MIPQ)[53].

5-{(4-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-ylsulfonyl)phenylamino)methyl}quinolin-8-ol (HTPSMQol) was synthesized by optimized reaction of 4-(6,7-dihydrothieno[3,2-
cpyridin-5(4H)-ylsulfonyl)aniline with 5-chloromethyl-8-hydroxy quinoline hydrochloride (CMHQ), by Paresh N. Patel et al. [54].

2.3. Reviews about Metal chelates of mixed ligand of 8-hydroxy quinoline:

Complex forming (Chelating) agents are becoming of increasing importance in analytical chemistry such as in gravimetric, titrimetric and colorimetric measurements. New types of complexes and complex forming agents are constantly under investigation, for possible analytical and industrial applications. The growing importance of the use of metal chelates in analytical chemistry may be realized by the ever-increasing number of publications on this subject. Some of recently repotted Metal chelates of mixed ligand of 8-hydroxy quinoline are listed below.

Hasmukh. Patel et all. synthesized novel bis-(bidentate)-ligand 5,5′-(3,3′-(phenyl methylene)bis(1H-indole-3,1-diyl)bis(methylene)diquinolin-8-ol)(PBIQ) by condensation of 5-chloromethyl-8-hydroxyquinoline hydrochloride with 3,3′-(phenyl methanediyl) bis(1H-indole) in the presence of a base catalyst. Coordination polymers of this PBIQ bis-ligand were prepared with Cu(II), Ni(II), Co(II), Mn(II), and Zn(II) metal ions [55].

Coordination polymers of a novel bis(oxine) bidentate ligand, namely 1,8-bis(8-hydroxyquinolin-5-yl)-2,7-dioxaoctane (BQDO), have been prepared with the metal ions Cu(II), Co(II), Ni(II), Mn(II), and Zn(II), by T. B. Shah et all [56].

R. B. Dixit et all. synthesized co-ordination polymers of novel bis oxine bidentate ligand namely 1,6-bis(8-hydroxyquinolin-5-yl)-2,5-dioxo-3-methyl hexane (BQDMH) with different metal ion like Zn$^{+2}$, Cu$^{+2}$, Ni$^{+2}$, Co$^{+2}$ and Mn$^{+2}$ [57].

New main-chain-type polymers of 8-quinolinol were prepared by organometallic polycondensation. They had a poly(aryleneethynylene)-type structure and exhibited photoluminescence. Chain structure were synthesized by Takayuki Iijima et all [58].

The poly(ester amide) (PEA) was prepared by polycondensation of 1,4-phenylenebisphthalamic acid and the epoxy resin diglycidyl ether of bisphenol-A. The PEA was then treated with 5-chloromethyl-8-quinolinol hydrochloride. The metal
chelates of PEAQ with Cu\(^{2+}\), Zn\(^{2+}\), Mn\(^{2+}\), Ni\(^{2+}\), and Co\(^{2+}\) metal ions were prepared by Arun Singh et all[59].

Yunhai Liu et all. Developed Solid phase extraction with an ion-imprinted cross-linked HQ-type chitosan resin provides an effective pre-concentration of uranium (VI) [60].

A new ligand, 5-[(5-(pyridine-4-yl)-1,3,4-oxadiazole-2-thyl]methyl]quinoline-8-ol (K), was synthesized by Kaushal K. Oza et all by base-catalysed reaction of 5-chloromethyl-8-hydroxyquinoline (CMQ) and 5-(pyridine-4-yl)-1,3,4-oxadiazole-2-thiol. The obtained ligand was reacted with transition metal salts to afford metal-containing Heterochelates[61].

A.S.A.Zidan et all. synthesized some Transition metal complexes with combination of Glycinyldithiocarbamate and 8-hydroxyquinoline moiety. 8- Hydroxyquinoline also reported to be active against bacteria. Derivatives of this ligand also play important role as polymerization inhibitors as well as analytical reagents in industry[62].

Mauro Ghedini et all. synthesized complexes formed by cyclopalla-dated 2-phenylpyridine co-ordinated to 5-substituted-8-hydroxyquinolines, are at room temperature and in fluid solution, luminescent with an absolute photoluminescent quantum yield which depends on the nature of the substituent in position 5[63].

New chelating copolymer (HQDMA) has been synthesized through
copolymerization of 8-hydroxyquinoline and dimethylolacetone monomers in the presence of base as a catalyst by T. B. Shahet all[64].

Shayma A Shaker et.all synthesized some Transition metal complexes with combination of 8-hydroxyquinoline and o-hydroxybenzylidene-1-phenyl-2-3-dimethyl-4-amino-3-pyrazolin-5-on[65].

Yong-chum et all. synthesized some complexes of Yb (II) with Schiff- base ligands derived from 8-hydroxyquinoline -2- carbaldehyde and four aroylhydrazines. The applications of synthesized compound in the area of bio medical science as well as in the area of biochemistry[66].

Kharadi et all. synthesized some Transition metal complexes of Cu (II) with combination clioquinol (5-chloro-7-iodo-8-hydroxyquinoline) and four different Coumarin derivatives ligands[67].

Shumei Zhai.Lei Yang et all synthesized some complexes of Cu (II) with 8-hydroxyquinoline moiety and clioquinol. They reported the applications of synthesized compound in the area of medical science[68].

Kharadi et all. synthesized some Transition metal complexes with combination clioquinol (5-chloro-7-iodo-8-hydroxyquinoline) and 1, 10-phenanthroline as ligands. Comparative analysis shown higher antimycrobacterial activity of the complexes and free ligands than metal salt[69].

Panchani et all, synthesized some coordination chain polymers of the type M(H2L)(H2O)2n.XH2O (where M = Mn(II), Cu(II), Zn(II), X=1;Co (II), Ni (II) X=2, H2L= 2.2’-bis-4-{(8-hydroxyquinolinolyl-5- methylenoxy)phenyl]propane}[70].
Kharadi et al. synthesized some coordination chain polymers of the type 
\[ ([M(QM1N)(H_2O)_2] \cdot H_2O) \_n \] (where M \( \equiv \) Mn(II), Co(II), Ni(II), Cu(II), Zn(II), QMIN 1,5-bis(8-hydroxyquinolinolyl-5-methylenoxy)naphthalene) ligands[71].

2.4. Research gaps about the reaction products of CMQ:

The reaction of CMQ with various nucleophilic reagents has been reviewed as above. It was noted that the reaction of CMQ with various alcohols has been reported [30] but so-called 5-Alkoxymethyl-8-quinolinoldervatives have not been employed for metal complexation study. Hence it was thought to study the chelating properties of such compounds.