SYNTHESIS AND CHARACTERIZATION OF BIOLOGICALLY IMPORTANT NOVEL QUERCETIN OXIME DERIVATIVES OF Pd (II) COMPLEXES

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ABSTRACT
We have developed a simple, convenient and effective method for the synthesis of different complexes of Quercetin oxime. The ligands and their complexes would be screened for their anti-cancer activity against certain cancer cell lines. All the compounds are supported by IR, NMR, ESR, Electronic spectral data.

KEYWORD: Quercetin oxime.

INTRODUCTION
The Oxime attracted our attention because they possess a broad spectrum of potentially useful chemotherapeutic properties. In recent years a considerable amount of research has been devoted to the synthesis of various substituted Oxime derivatives. Most medicinal compounds possess one or other heterocyclic ring. The isooxazole and their derivatives are widely present in nature and not only one of the most important heterocyclic compounds in organic chemistry, but also building blocks which are essential for the total synthesis of the complicated naturally occurring metabolites.

Phytochemicals like Quercetin and their derivatives are generating great interest, as the sources of natural due to their potent biological activities like anti-oxidant, anti-tumor and anti-cancer activities. Quercetine oxime derivatives and their complexes with various metals are known to possess wide range of biological and pharmacological activities. In the present work, an attempt has been done to synthesize and characterize Oxime derivatives of Quercetin and their metal complexes.
The herbal traditional medicinal plants, are important raw material to prepare or synthesis the phyto-chemicals.\textsuperscript{[1]} The phytochemical, Quercetin is one of the major dietary Flavonoids, belonging to a group of Flavonols.\textsuperscript{[2]} Flavonoids have a long history of use in traditional medicines in many cultures, but Flavonoids themselves were not discovered until the 1930s\textsuperscript{[3-5]} Research in recent years has focused on several possible helpful effects of Quercetin, including its potential role in preventing cancer. Quercetin appears to have anti-tumor and anti-oxidant properties. Recent studies suggest that Quercetin can slow the growth of cancer cells.\textsuperscript{[7]} These types of studies are not as conclusive as clinical trials. One clinical study of people with a strong inherited tendency to develop colorectal cancer found that the combination of Quercetin and curcumin supplements decreased the number and size of precancerous rectal tumors. Traditionally used medicinal plants produce a variety of compounds of known therapeutic properties. Plants used in ethno medicine for the production of bioactive compounds are used and rationalize the use of these medicinal plants in health care.

A large number of thiosemicarbazone have been evaluated for their anti-malarial and anti-tumor activities, because of their useful chemotherapeutic properties. In cancer treatment it has been shown that the metal chelates are more potent than the chelating agents.

![Thiosemicarbazide](image)

Metal complexes of palladium containing nitrogen and oxygen donor ligands is found to be effective catalysts for oxidation, reduction, hydrolysis and other organic transformation.\textsuperscript{[6]} The redox properties of the Quercetin derivatives has been found to block cell cycle progression in a variety of malignant cell lines including those derived from the prostate, brain, breast, pancreas and colon. Quercetin derivatives vincristine and vinblasine is mainly useful for treating Hodgkin’s disease, lymphocytic lymphoma, advanced testicular cancer and advanced breastcancer. Scientists of the Henan University, China, concluded that Quercetin
could improve therapeutic index of doxorubicin, a drug used in cancer chemotherapy. Due to its Anti-oxidant Activity, rutin protects liver cells.

![Rutin structure](image)

The phytochemicals, when administered to rats, rutin has also been found to display chemopreventive properties, acting as an agent blocking carcinogenesis induced by heterocyclic amines.[8-16]

**Chemicals and reagents**

All the reagents used in the preparation of ligands and their metal complexes were of reagent grade (Merck). The solvents used for the synthesis of ligands and metal complexes were distilled before use. All other chemicals were of AR grade and used without further purification.

**Synthesis of Ligand**

A $1 \times 10^{-3}$ M solution prepared by dissolving appropriate amounts oxime in 50ml methanol and 2ml of glycial acetic acid was added drop wise to a $5 \times 10^{-2}$ M solution of Quercetin in 50ml methanol while stirring and refluxed for 2-3 hours the product that separated was recrystallized was based on elemental analysis, via, FT-IR HNMR, C NMR, ESR, U.V methods.
The fourth chapter describes the synthesis of Quercetin Oxime metal complexes analogues and their antioxidant, antitumor, antifungal, anticancer biological activities. The literature survey reveals that the metal complexes of active drugs as Mg and can have important pharmaceutical properties. Complexation with metal can reinforce the activity of the compound by the combination of effects from the ligands and from the metal residue. The activity of transition metal \{Au(III) and Ru (II)\} were introduced into the molecular structure and the reaction of appropriate metal precursor.

**Synthesis of metal complex**

To 30ml of metal solution (5x10^{-2} M) methanol was added (1x10^{-2} M) Quercetin oxime in methanol and the mixture refluxed for about 1 hour in a separate reflux arrangement. The solid that separated was filtered and washed with water and recrystallized with methanol.
BIOLOGICAL ACTIVITY

The nuclease activity of present ligands and their complexes has been investigated on pBR 322 plasmid DNA by agarose gel electrophoresis in the presence/absence of H2O2. At micromolar concentration, the ligands exhibit no significant activity in absence and in the presence of the Oxidant, which may be due to free radical reaction (OH*) with DNA. The production of hydroxyl radicals due to the reaction between H2O2 and the metal complexes. The OH* radical involves oxidation of deoxyribose moiety followed by hydrolytic cleavage of sugar phosphate backbone.
CONCLUSION
We have developed a simple, convenient and effective method for the synthesis of different complexes of Quercetin oxime. The ligands and their complexes would be screened for their anti-cancer activity against certain cancer cell lines. All the compounds are supported by IR, NMR, ESR, Electronic spectral data.

REFERENCES
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