

ABSTRACT

Charles University in Prague

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology & Toxicology

Candidate: Klára Bechná, MSc.

Consultant: Ass Prof. Přemysl Mladěnka, PharmD., Ph.D.

Title of Thesis: Copper chelating properties of 8 - hydroxyquinolines

Copper is an essential trace element in our body, which is involved in many physiological reactions. Disruption of copper homeostasis is associated with various pathological states. And thus copper chelators represent in these cases an important treatment strategy. Research for new active compounds like copper chelators can push the boundaries of the treatment of many hardly treatable diseases like Alzheimer's and Wilson's disease or cancer.

This thesis presents a study of the chelating properties of a class of compounds derived from 8 - hydroxyquinolines. These substances chelate metal ions including copper ions and have various biological properties ranging from antibacterial to anticancer effects. Clioquinol and other substances from the group of 8 - hydroxyquinolines effectively block the formation of oligomeric β - amyloid associated with the progression of Alzheimer's dementia and can present a potential modern method for the treatment of this disease.

In the experimental part of the work we tested the degree of chelation for all investigated substances by a simple but precise and proven methodology. Tested substances, clioquinol, cloroxine and 8 - hydroxyquinoline reacted with cuprous or cupric ions and formed complexes. Spectrophotometric measurements provided us the results about the chelating properties of the substances. These compounds were also tested for their reducing potential.

The highest and identical chelating ability were observed for both clioquinol and cloroxine. They produced stable complexes, at all tested pH and with stoichiometry of 2:1, tested chelator:copper. 8 - hydroxyquinoline not produce stable complexes and chelating activity was highly affected by the ambient pH. All compounds reduced the spontaneous reduction of cupric ions in all tested conditions.

In conclusion, we have verified chelation ability in all tested substances. In both halogen derivates, clioquinol and cloroxine, stable complexes with copper, both in acidic as well at physiological pH was confirmed.

ABSTRACT

Charles University in Prague

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology & Toxicology

Candidate: Klára Bechná, MSc.

Consultant: Ass Prof. Přemysl Mladěnka, PharmD., Ph.D.

Title of Thesis: Copper chelating properties of 8 - hydroxyquinolines

Copper is an essential trace element in our body, which is involved in many physiological reactions. Disruption of copper homeostasis is associated with various pathological states. And thus copper chelators represent in these cases an important treatment strategy. Research for new active compounds like copper chelators can push the boundaries of the treatment of many hardly treatable diseases like Alzheimer's and Wilson's disease or cancer.

This thesis presents a study of the chelating properties of a class of compounds derived from 8 - hydroxyquinolines. These substances chelate metal ions including copper ions and have various biological properties ranging from antibacterial to anticancer effects. Clioquinol and other substances from the group of 8 - hydroxyquinolines effectively block the formation of oligomeric β - amyloid associated with the progression of Alzheimer's dementia and can present a potential modern method for the treatment of this disease.

In the experimental part of the work we tested the degree of chelation for all investigated substances by a simple but precise and proven methodology. Tested substances, clioquinol, cloroxine and 8 - hydroxyquinoline reacted with cuprous or cupric ions and formed complexes. Spectrophotometric measurements provided us the results about the chelating properties of the substances. These compounds were also tested for their reducing potential.

The highest and identical chelating ability were observed for both clioquinol and cloroxine. They produced stable complexes, at all tested pH and with stoichiometry of 2:1, tested chelator:copper. 8 - hydroxyquinoline not produce stable complexes and chelating activity was highly affected by the ambient pH. All compounds reduced the spontaneous reduction of cupric ions in all tested conditions.

In conclusion, we have verified chelation ability in all tested substances. In both halogen derivates, clioquinol and cloroxine, stable complexes with copper, both in acidic as well at physiological pH was confirmed.

ABSTRACT

Charles University in Prague

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology & Toxicology

Candidate: Klára Bechná, MSc.

Consultant: Ass Prof. Přemysl Mladěnka, PharmD., Ph.D.

Title of Thesis: Copper chelating properties of 8 - hydroxyquinolines

Copper is an essential trace element in our body, which is involved in many physiological reactions. Disruption of copper homeostasis is associated with various pathological states. And thus copper chelators represent in these cases an important treatment strategy. Research for new active compounds like copper chelators can push the boundaries of the treatment of many hardly treatable diseases like Alzheimer's and Wilson's disease or cancer.

This thesis presents a study of the chelating properties of a class of compounds derived from 8 - hydroxyquinolines. These substances chelate metal ions including copper ions and have various biological properties ranging from antibacterial to anticancer effects. Clioquinol and other substances from the group of 8 - hydroxyquinolines effectively block the formation of oligomeric β - amyloid associated with the progression of Alzheimer's dementia and can present a potential modern method for the treatment of this disease.

In the experimental part of the work we tested the degree of chelation for all investigated substances by a simple but precise and proven methodology. Tested substances, clioquinol, cloroxine and 8 - hydroxyquinoline reacted with cuprous or cupric ions and formed complexes. Spectrophotometric measurements provided us the results about the chelating properties of the substances. These compounds were also tested for their reducing potential.

The highest and identical chelating ability were observed for both clioquinol and cloroxine. They produced stable complexes, at all tested pH and with stoichiometry of 2:1, tested chelator:copper. 8 - hydroxyquinoline not produce stable complexes and chelating activity was highly affected by the ambient pH. All compounds reduced the spontaneous reduction of cupric ions in all tested conditions.

In conclusion, we have verified chelation ability in all tested substances. In both halogen derivates, clioquinol and cloroxine, stable complexes with copper, both in acidic as well at physiological pH was confirmed.