CE - 4

INORGANIC SYNTHESIS OF Cr(III)- BASED ANTIHYPERGLICEMIC AGENT AS A LEARNING RESOURCE OF THE BIOINORGANIC CHEMISTRY SUBJECT : BRINGING THE LABORATORY INTO THE CLASSROOM

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Abstract

Many examples showed of the effectiveness of inductive and hands on learning. The excellent place to encourage this type of learning is Laboratory experiments. Experimental synthesis of antihyperglicemic agent based on Cr(III) complex is an empirical experience which can bring the student to understand how to obtain biologically active ingredients in bioinorganic chemistry. This is a part of an Inquiry-Based Science Classroom. It will give an additional benefit of mixing laboratory activity with classroom learning and problem solving in a more practical approach than a separate laboratory and lecture.

Key words: Inductive learning, laboratory experiments, Bioinorganic Chemistry, Antihyperglicemic Agent, Inquiry-Based Science Classroom

INTRODUCTION

Bioinorganic Chemistry is a subject which will teach the student the important role that metal ions play in key biological processes. Some topics include electron transfer; carbon, oxygen, and nitrogen metabolism; metal uptake and trafficking; biomineralization; metals in medicine and metal toxicity (Bertini, 2007). Both written and oral scientific communication are stressed. Some illustration were needed in order to get the sufficient understanding. This subject is the answer of these questions : What is the role of Inorganic Chemistry in biological life? How the inorganic species' do their activities in whole nature?

DISCUSSION

1. Bioinorganic Chemistry

In the Bioinorganic Chemistry subject, student will learn that many biological functions are performed at the cellular level by metal ions that are incorporated into the activation sites of proteins and enzymes. For example, when oxygen is transported through blood in the human body, it is bound to iron ions that are incorporated into the hemoglobin protein (Scarrow,2007). The progress through this course, there are some topics about these and other requirements and mechanisms that must be present in order to facilitate critical biological functions. Students begin

this course by reviewing the basic principles of inorganic chemistry, biochemistry, and molecular biology. Following a brief overview of the spectroscopy methods that scientists use in the study of metals that contain protein, student will explore the structures of the most relevant metal centers in biological molecules, focusing in particular on non-redox enzymes, electron-transfer copper-based and iron-based proteins, nitrogen-fixation proteins, nitrification and denitrification proteins, and oxygen-transporting proteins. This course will help student to recognize the importance of inorganic molecules in supporting organic biological systems. As the progress through this course, student not only will gain an understanding of some very complex macromolecules that rely on metal centers; but also will gain insight into recent scientific developments that utilize key metal ions for breakthrough medical purposes (Cowan, *1997 ;* Crighton, 2008).

Some question in Bioinorganic Chemistry are as follows (Scarrow, 2007) :

1. What is the biological function and/or medical relevance of the system? In what species is this system found, and from which species is the system best characterized? If this a
2. protein, is it part of a family of related proteins, and if so, what are some of the names ofthe similar proteins?
3. What is the metal involved?
4. What is the coordination environment of the metal?
5. What is known and generally accepted about the chemical role of the metal and its coordination environment in carrying out the function of the system?

2. The role of Cr(III), a case study

One of the main topics in Bioinorganic Chemistry is "metals in medicine'. The explanation of this topic is that some metal complexes or organo-metallic compounds have been used in medicine for centuries. Metal complexes play essential role in pharmaceutical industry and in agriculture. The metallo-elements present in trace quantities play vital roles at the molecular level in living system. Inorganic compound or metal-containing medicinal product may contain a specific medicinal purposes, for example platinum as antitumor agents (Roat-Malone & Rosette, 2002). In diabetes, intake of chromium metal complex shown considerable reduction in the glucose level (Anderson, 2000).

Diabetes is a metabolic disease which characterized by hyperglycemia and glycosuria resulting from the defect of the secretion or the action of insulin, or both of them (WHO, 2009). The particular management of diabetes included diet, exercise, supplement or nutraceutical, oral hypoglycemic agents and insulin are Nutraceuticals (often referred to functional foods) are natural bioactive or chemical compounds that have health promoting, disease preventing or medicinal properties (Pandey, 2011)**.** Most nutraceutical usually come from organic compounds. The inorganic nutraceutical is less popular.

Chromium(III) is a trace mineral which has an important role in glucose metabolism. The diabetes relevant interaction of Cr (III) is with the hormone insulin and its receptors. Cr (III) acts with insulin on the metabolism of sugar when entry into the cell, and facilitates the interaction of insulin with its receptor and the cell surface. Chromium increases insulin binding to cells, insulin receptor number and activates insulin receptor kinase leading to increased insulin sensitivity (Cefalu 2004; Feng, 2007). Activity of Cr-amino acid complex as was studied by Staniek et al., (2011) with the acute toxicity of Cr-glicynato complex.

The daily intake of Cr(III) intake is about 200µg. Chromium picolinate, $Cr(pic)_3$, is the most popular chromium supplement. It is a relatively well absorbed form of chromium (III). The disadvantage of $Cr(pic)_3$ is the effect of this compound in DNA damage. The search for compounds with novel properties to deal with the disease condition is still in progress (Hepburn, 2003; Vincent, 2012)

Ochiai (2008) reported that some amino acids with Cr(III) act as a part of GTF (*Glucose Tolerance Factor*). GTF is a low molecular weight Chromium (LMWCr) involved in the action

of insulin in processing glucose into energy. It is an oligopeptide of consists of glycine, cysteine, aspartate and glutamate with the acidic amino acid. A solution which contain chromium (III), glycine, glutamic acid and cystein mimics the biological activity of the naturally occurring GTF. There is a relationship between chromium (III) - amino acids complexes with GTF activity (Vincent, 2007). The research for compounds with ability to maintain the blood glucose level or called 'antihyperglycemic agent' is still in progress. The activity of novel Cr (III) compounds were studied as antihiperglicemic supplement. A previous study reported the synthesis of a Cr (III) complex an the activity as insulin mimetic (Yasarawan,2013).

A study on the synthesis of Cr(III)-amino acid and acids complexes is so important. Some previous studies reported the synthesis of some Cr(III) complexes (Rasuljan 1989; Yang 2005; tawkir 2012). Budiasih et al (2013)[(1)] was reported the synthesis of Cr-amino acids complexes in order to obtain a definitive and reproducible method and consistent product. Some modification applied to the previous procedures (Yang, 2005, Tawkir, 2012). The formation of the Cr(III) complexes was achieved by reaction of the ligand with these salts by reflux method. The occurrence of reaction was indicated by color changes from green to purple. The optimum condition is reflux at 80 ^{o}C in an hour the pH is 4. The yield were 40,08–87,50 % and 17,13-62,83 % Simulation of some instrumental data give the molecular formula, which is generally stated as **$[Cr(\mu\text{-}OH)(aa)_2(OH)_2]_2.6H_2O$.**

These complexes were proposed as antihyperglicemic agent. The in vivo experiment was studied on Streptozotocin (Stz) – nicotinamide induced diabetic Wistar rats. Investigation in 9 weeks on the treatment groups give significant effect in lowering glucose level compared to diabetic rats control group. All the Cr-amino acid complexes applied in this research have an antihyperglicemic activity on Nicotinamide-Sreptozotocin induced diabetic Wistar rats which expressed as % glucose lowering (%GL). The activity of Cr-amino acid complexes were 57.566 % for glutamic complex, 52.327% for glycine and 45.817% for cysteine complex, respectively (Budiasih et al., 2013)[(2)].

3. Bringing the Laboratory into the "Bioinorganic Chemistry" classroom

In most science courses and curriculum the classroom and the laboratory are separated in both time and space. Even when the laboratory is part of an individual course, it is still generally separate from the classroom portion of the class. This separation is usually necessary due to the difference in resources and time required for the various laboratory vs. classroom course activities. In addition, this separation has often resulted in excellent classes and laboratories. To teach using the structure of experiential learning cycles and to teach with an awareness of varied student learning styles, mixing lecture and laboratory is an advantage.

The use of laboratories is one of the distinctive features of engineering. Wankat and Orevitz1 suggest several goals that laboratories can meet including motivation and problem identification, discovery, induction, experience with equipment, real world type experiences, the opportunity to However if there is too much separation between the students working on an unknown problem and them finding a solution, it can lead to frustration. A laboratory in the classroom allows students to see a problem and be quickly led toward a solution. In many cases instructors begin to bring the laboratory into the classroom through demonstrations or maybe a trip to the laboratory. It called inductive learning, which begin with particulars and build to generalities. (Moor & Piergiovanni, 2003).

The inductive approach is the way most things are discovered and clearly how an infant learns, but it is not the way most courses are taught. Therefore, it requires differently thingking about how we approach the classroom. Experiments are an excellent way to provide concrete particulars to begin inductive learning.

The following sequence in using experiments in inductive learning are :

- Prelab Handout - Students are given a handout to peak interest that asks them to hypothesize about qualitative outcome.
- Data Collection – Students complete experimental work consisting primarily of data collection with graphical analysis.
- Discussion – Students identify key patterns and experimental relationships.
- Lecture – Students are presented with key quantitative relationships.
- Homework – Students are asked to complete calculations based on the laboratory data

This inductive approach contrasts with the usual deductive approach where we would generally start with the lecture and homework and then follow up with an experiment. Completing the experiment in class facilitates using this type of sequence.

Topic in Bioinorganic chemistry subject, like at another subject in science, is moving more rapidly than ever and must understood empirically. An innovative science teaching is needed for communication between science teachers, practising scientists and other stakeholders in science education. For example, how to provide the role of some metal in medicine? Finding it by their own work will give a high retention in student's understanding. This is commonly called an inquiry based learning. In the science course it can stated as an Inquiry-Based Science Classroom.

Teaching in an Inquiry-Based Science Classroom needs a special approach. One of an Inquiry-Based Science Classroom method is bringing the laboratory into the classroom. The most important things in this method are the ABCs (attitudes, behaviours and competencies) of the teachers. The stage for teaching and active learning was created as good as possible . It is the role of the teacher to stimulate and nurture the curiosity of their student (Llewellyn, 2005).

This method needs to balance the equipment prepared for lessons, to book equipment and resources, with a desire to be able to respond to student questions by enabling them to suggest activities and investigations. Not all students and teachers are ready to begin with full student inquiries at the start of the school year. During the first few weeks of school, teachers need to establish expectations for classroom management, laboratory practices and routines. Without taking the time to establish some essential guidelines, inquiry classrooms can become unruly and unmanageable (Llewellyn, 2005)

Some tips teachers can do to integrate Common Core standards into their lesson plans are (Hughes 2013) :

a. Use technology to work collaboratively.

Students must think critically under Common Core — examining complex, real-world subjects in a multifaceted way and then working together to solve the resulting problems.

b. Make books come alive online.

Using free downloadable files can help students make interdisciplinary connections required by Common Core.

c. Teach web-searching skills.

Internet treasure hunts help students search for information.

d. "Flip" the classroom.

In the flipped classroom, new information is presented outside of class as homework instead of in a traditional lecture, encouraging students to learn at their own pace and dig deeper into material.

e. Making a learning video game.

This is a great way to teach real-world math concepts. A programs such as Trimble SketchUp that use geometry to teach building design. Teachers and students can also use free video game-design software to create multimedia lessons.

f. Teach in teams.

The interdisciplinary nature of Common Core encourages teachers to work

collaboratively across subjects

g. Encourage note taking.

It requires more focus on analysis of texts, such as news articles and government reports, an essential skill for college and careers. Teacher can teach text analysis through annotations, commenting on complex texts in real time.

h. Practice assessment tests.

Do it using the consortium's sample test questions and answers in class.

i. Bring the experimental strategies to the classroom discussion

The sequence of inductive learning is applied in the relevant topic.

Some reasons make an inquiry class different. The role of the teacher and the student sets inquiry based learning apart from other ways of teaching and learning. In an inquiry based classroom student and teacher were act and get several special gains.

Strategies for Implementing Laboratories in the Classroom include some approach (Moor & Piergiovanni, 2003 :

a. Strategy 1: Experimental Demonstrations
b. Strategy 2: Dry-lab (Thought) Experiments
c. Strategy 3: Simple experiments in a traditional classroom:
d. Strategy 4: A classroom designed for combined experiments, lectures and problem solving

These methods will make student and teacher feel and do anything as follows (Llewellyn (2005) :

Students	**Teachers**
are interested and engaged	are interested and engaged
are researchers / investigators	are also enthusiastic learners
view themselves as scientists	use effective pedagogies for students engagement and development of understanding
engage in investigations that develop from their own questions	support students seeking to investigate their own questions, providing encouragement while maintaining safe operating procedures
use evidence to substantiate claims	use effective questioning to encourage the development of higher order thinking.
use high order thinking skills	provide opportunities for metacognitive strategies
connect new knowledge and prior learning	identify prior knowledge of students and use this as a basis for learning/teaching act as reflective and critical friends to their peers
seek and use many sources of information e.g. mentors / experts, internet, text and multimedia,	seek evidence that a variety of sources have been consulted to elicit information

In the case study of chromium, students learn that there is a significant difference between Cr(III) as antigyperglicemic agent in contrary with the analogue chromium species, the Cr(VI), as a toxic substance. The active species was related to the molecular formula of the compound and how these compound were synthesized. In vivo investigation of the hyperglycemic activity is an example of an inquiry based science classroom It provides the answer of the main question

about the role of Cr(III) in the topic : "metal in medicine" of the Bioinorganic Chemistry course.

Reducing the barriers between the laboratory and the classroom can help facilitate inductive learning, the structuring of experiential learning cycles and the diversity of teaching approaches. The classroom based laboratory exercises help set up active experiences that give students improvel of their learning experience.

CONCLUSION AND SUGGESTION

The antihyperglicemic activity of Cr(III)-amino acids complexes and include the synthesis method is a special case which closely related to the one of main topic in Bioinorganic Chemistry : **metals in medicine.** Bringing the information from the laboratory into the classroom can improve the student's involvement and understanding in this topic.

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