Original Article

Using Simple Modeling Experiments and Basic Materials to Illustrate Proteins and Enzymes Structure and Function for Medical Students

Durdi Qujeq Ph.D.

Dept. of Clinical Biochemistry, School of Medicine, Babol University of Medical Sciences, Babol, Iran

Address for Correspondence: Dept. of Clinical Biochemistry, School of Medicine, Babol University of Medical Sciences, Babol, Iran, Zip-code: 47176-47745, Tel: +981132190569, Fax: +981112290181, Email: dqujeq@gmail.com, d.qujeq@mubabol.ac.ir

(Received: 6 Oct 2014 Accepted: 7 Apr 2015)

Abstract

Introduction: Misunderstanding enzyme structure and function is a major problem of biochemical education. The purpose of this work was to consider the general features of structure and function of proteins and enzymes relevant to an understanding of structure and function of proteins and enzymes by modeling experiments.

Methods: A total of 109 medical students of Babol University of Medical Sciences during a few years were recruited to participate in the study. The data were obtained by a researcher-made questionnaire. Totally 89% of the students participated in the study, and finally 109 questionnaires were completed.

Results: After intervention, the mean scores of proteins and enzymology were significantly higher than before it. There is a significant difference in Mean examination scores of the medical students before (14.2±1.4, 14.9±1.2) and after (17.2±1.6, 18.3±1.3) the intervention for male and female students, respectively, in terms of using proteins and enzymes structure modeling. Also, a brief outline is given of those aspects of proteins and enzymology which are most relevant to clinical practice,(I) to illustrate some aspects of proteins and enzymes structure, and (II) allow students to become skilled in processing, presenting and discussing data obtained directly by them, or furnished by the instructor.

Conclusion: This simple method can be successfully used to illustrate, explain and characterize many of the physical, chemical and clinical properties of proteins and enzymes. It can also be looked upon as a method for assessment of the education quality, preferably through experiences in medical education.

Keywords: Enzyme, Proteins, Structure, Education, Medical students

Citation: Qujeq D. Using simple modeling experiments and basic materials to illustrated enzyme structure and function for medical students. Educ Res Med Sci. 2015; 4(1): 8-13.

Introduction

Enzymes are biological catalysts. All enzymes are proteins. Also, enzymes share certain structural and functional features irrespective of the reaction catalyzed. Enzymes contain a functional site, called the active site, where reactants are converted to products (1, 2). Enzymes catalyze in a highly specific way, chemical reactions taking place within the living cell. Often a further, non-protein, component called a cofactor is required before an enzyme has catalytic activity. Many enzymes contain prosthetic groups that are non-amino acid in nature (3, 4). The conjugated protein is known as the holo-enzyme and can be dissociated into a protein

component, the Apo-enzyme, and its non-protein prosthetic group, the cofactor (5). Enzymes are highly specific for the reactants, or substrates, they act upon. Substrate molecules are bound inside a somewhat hydrophobic cleft known as the active site, which is often located between two domains or subunits of a protein or in an indentation, such as a pocket at one end of a barrel (6). All living processes are in some way regulated by the presence of enzymes. The correlation between structure and function is one of the most relevant topics in biochemistry and molecular biology, and through detailed study of protein structure it is possible to understand how a macromolecule works (7). This is taught at the beginning of the first semester in medical schools. Medical students find basic biochemical concepts difficult to relate to real life but hope to learn how to apply them in medicine (8, 9). Usually they are not open to learn these biological concepts. In the learning of fundamental biochemistry, as in any other area, much extra class work is required before students fairly understand concepts concerning enzyme structure and properties (10, 11). Flexible and creative teaching techniques are used to increase students' interest. It is true that enzyme structure developing methods in biochemistry provide a new prospective on biochemistry (12, 13). It was found that the developed models could predict the COX-2 and COX-1 inhibitory activities (14). Understanding the structure and function of enzyme for medical students is very difficult. The simple and useful method here described can be effectively used to evaluate the student understanding and to convey effectively, several concepts involved in enzyme structure. Thorough discussion of the method clarifies enzyme structure and enhances understanding in most students. This work is to provide a comprehensible account of those aspects of enzymology relevant to an understanding of structure and function of enzymes. The aim of this paper is to use modeling experiments and basic materials to illustrate enzyme structure and function to be introduced to medical students.

Methods

This cross-sectional study included 109 medical students (68 female and 41 male) in Babol University of Medical Sciences. The interval data examined was mean examination score during a few years. These data were compiled in a database, and analysis was performed using SPSS statistical software version 21.0. Mean values were calculated as Mean±SD. Statistical significance was defined as $P<0.05$.

Enzyme and Proteins structure

Students worked in groups of 5 under demonstrator supervision. To learn the structure of the proteins and enzymes, different colored paper was used. Models of the proteins and enzymes were made from thick bored and different cloth was used for the substrate, active site and inhibitor. A strand of thread connected them. The substrate, active site and inhibitor were colored in different forms. Amino acid residues connected by strands of thread as already described illustrate the structure of the proteins and enzymes. That model easily demonstrated the flexibility of proteins and enzymes structure. Students familiarized themselves with different inhibitors and learned about the active site. They were interested in proteins and enzymes clinical properties and basic kinetics. They were very happy working in small team to do this work.

Formation of enzyme active site

The active site is responsible for binding the substrate and for operating chemically on the substrates to catalyze their transformation to products. Enzymes possess an active site that is a small portion of the entire protein. Enzyme – catalyzed reactions occur at an asymmetric pocket of the enzyme called the active site. The conformation and chemical composition of the active site determines the specificity of enzymatic catalysis. The active site can be subdivided into a binding site, which includes the amino acid residues that come into contact with the substrate and a catalytic site, which includes residues directly responsible for catalysis. To illustrate enzyme structure more than 100 amino acid residues are connected together by a strand of thread. This simple approach made students more familiar with the variety of amino acid residues in the structure of an enzyme. They learned about N and C terminals, the numbering of amino acids, and amino acid sequences in enzymes. They enjoyed working on a model of many kinds of enzymes such as Amylase, Transaminases and phosphatase. Moreover, they learned about the function and clinical importance of some especial enzymes such as creatine kinase and lactate dehydrogenase. They became familiar with enzyme structure and experienced cooperative teamwork.

Conformation of the enzyme

The interactions between residues that produce the three-dimensional shape of an enzyme and protein include: hydrophobic, electrostatic, hydrogen bonding, and disulfide bonding. Students used colored springs to make the connection between H and N atoms. The students connected the carbon of one amino acid to the nitrogen of another. Also, they produced a linkage between H, N

and/or O atoms with a spring wire and showed hydrogen bound in the secondary structure of enzymes as well as α-Helix and β-Pleated sheet. Therefore, they could configure easily the internal and external hydrogen bound, α-helix and β-Pleated sheet structure. It was very exciting for the students to see the internal and external bindings of hydrogen in enzyme and protein structure.

Enzyme properties and kinetics

A number of factors destroy enzyme activity as a consequence of their ability to denature proteins, that is to produce an extensive disturbance of the three dimensional structure of the enzyme. Denaturing agents include heat, extremes of pH, organic solvents, and detergents. Forces that produce the three-dimensional conformation of an enzyme include electrostatic and hydrophobic interactions and hydrogen and disulfide bonds. Besides using a strand of thread for covalent amino acids into a polypeptide and colored springs for hydrogen bound between H and N atoms, students used colored wire to show the effect of denaturing agents. The students used colored wires to show effects of denaturing agents and compression and decompression of active sites. They could experience the effect denaturing agents by pressing and releasing amino acid residues (abduction and adduction of enzyme structure). Also, they illustrated a three dimensional form of proteins and enzymes in tertiary structure. They could show spatial form structures of proteins and enzymes.

Multiple forms of enzyme

The dehydrogenase structures are an excellent example of the use of pleated sheet; helical and random coil regions in a globular protein. Human alcohol dehydrogenase is a dimmer and is polymeric being formed from three different subunits. The students compared alcohol dehydrogenase and dehydrogenase structures as quaternary structure of enzymes. For illustration of quaternary structure, the students stuck many envelopes on a A4 paper sheet and put a button in each of the envelopes that represented active site. Also, to show the position of the inhibitor, a colored button was stuck outside the envelopes; then by using a strand of thread, these two buttons were connected to each other. Therefore, it was shown that an enzyme contains many envelopes and inhibitors whereas enzyme molecules contain only one envelope (active site).

Statistical analysis

The data were analyzed by the SPSS version 21.0, and results were expressed as mean value ± SD. A P-value<0.05 was considered significant.

Results

Mean examination scores of the medical students in proteins and enzymology section before and after using the proteins and enzyme structure modeling is shown in figure 1.

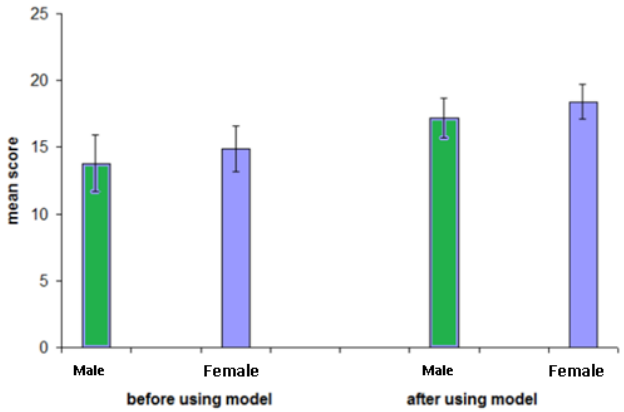

Figure 1. Mean examination scores in protein and enzymology section of the medical students before and after using enzyme structure modeling

Also, this approach permitted students to visualize the active site, inhibitors, and enzyme structure. The most important property of an enzyme is its catalytic activity. As a consequence of the protein nature of enzymes, this catalytic activity is influenced by a large number of factors. These include the nature of the substrate, temperature, pH, conditions that alter protein structure and the presence of other molecules.

It is a simple and useful application of model building to the understanding of enzyme structure. It offers particular advantages for teaching this at the medical student's level. Students showed great interest and enjoyed learning about structure of different enzymes. It was very satisfying for them as they were involved in a cooperative and pleasurable activity. An example of an exercise handed to the medical students is shown in table 1-3.

Table 1. Exercise 1: Study on nature of active site and induced fit.

Model feature used	Tasks
Display modeling of enzyme structure. Show backb	What can you conclude about the amount of amino acids involved in the active site of the enzyme? Look for N-terminal and C-terminal in proteins and enzymes.
Show enzyme folding.	How the substrates influence the conformation of the enzyme? Explain how specific amino acid could stabilize and destabilize the different primary, secondary, tertiary and quaternary structure of proteins and enzymes and identify the amino acids involved in it.
Show H bonds in enzyme.	Compare the hydrogen-bonding patterns characteristic of α-helices and β-sheets in proteins and enzymes. Select a helix and identify the amino acids involved in proteins and enzymes. How is the amino acid side chains accommodated in an α-helix?
Show S-S bonds, display backbone.	Visualize the S-S bonds and look for the amino acids involved in the proteins and enzymes at extent do these bonds contribute to stabilize the globular structure?

Table 2. Exercise 2: Study on enzyme properties and kinetics

Model feature used	Tasks
Display initial rate	What is the maximum rate (Vmax) and the Michael's constant (Km)?
Show effect of PH and amount of enzyme	What is the relation between the rate of enzyme and pH?
Show kinetics	What is the Michaelis - Menten equation

Table 3. Exercise 3: Study on enzyme inhibition.

Model feature used	Tasks
Display modeling of enzyme inhibition.	What kinds of substrate inhibit enzyme and reduce the initial velocity? Identify mechanism of the inhibition.
Show inhibitors	What is the chemical nature of the inhibitors?
Show sequence	According to the primary sequence, what can you conclude about to the position of the inhibitors involved in the enzyme?

Discussion

The main finding of this study indicated that there is a significant difference in mean score of proteins and enzymes section before and after the use of proteins and enzymes structure modeling. This paper demonstrated the simplicity and versatility of the proteins and enzymes section for medical students by using the present educational method. Also, in our experience this teaching method has been very efficient in identifying misunderstanding of proteins and enzymes structure, to follow up new concepts development, and to reinforce fundamental concepts. Our results are also similar to those of other investigators (3). Moreover; the students are stimulated to recall concepts of proteins and enzymes structure and to associate them with enzyme properties and behavior. Also, they enjoyed teamwork, and then they took part in class discussions, so they were very active in

the class and could get a good score on the final exam. In addition, this paper gives a guided tour of the teaching on proteins and enzymes structure at the university for first year medical students. Besides, this work gives the students an additional interest and motivation for proteins and enzymes structure education. One of the most important points of the present research was that 93.5% of the medical students believed that the present method provide the necessary knowledge to them in order to understand enzymes mechanisms. The results of our experiments are in agreement with those reported by other investigators (3,5), but they were not in good agreement with those reported previously (4).The exercises proposed here offer particular advantages for enzyme structure teaching, and also for teaching structural molecular biology at the medical student level. Our experience with this teaching model indicates that students show great interesting biochemistry concepts.

After using this method, student learned that formation of the enzyme–substrate complex can occur only if the substrate possesses special groups, which are in the correct three-dimensional arrangement to interact with the binding groups of active site. They also, learned the catalytic activities of many enzymes depend on the presence of components called cofactor. Students examined that the hydrogen ion concentration can have a marked effect on enzyme activity because many of the amino acids in the enzyme bear ionize-able groups. Also, medical students learned the basic conceptual background that will allow them to understand disease mechanisms. In the first step, they selected the proteins and enzymes structure with the greatest clinical relevance. The second step was an attempt to present that information in a way that optimally facilitated learning and retention.

Conclusion

Developed simple method of teaching structure and function of proteins and enzymes to medical students was useful. Using this method showed that the proteins and enzyme biology sections for medical students is very simple and understandable. However, more research is needed in order to confirm the role of modeling as a useful educational method.

Acknowledgments

I wish to acknowledge the important input received from our medical students of Biochemistry Course. I am also grateful to the staff of the Faculty of Medicine, Medical University of Babol. This study was supported by an award grant from Research Council of University (no: 9237310).

References

1. Whiteley CG. Enzyme kinetics: Partial and complete uncompetitive inhibition. Biochem. Educ. 2000; 28(3): 144-147.

2. Cameselle JC, Cabezas A, Canales J, Costas MJ, Faraldo A, et al. The simulated purification of an enzyme as a 'dry' practical within an introductory course of biochemistry. Biochem Educ. 2000; 28(3): 148-153.

3. Sansom CE, Waller DA, Geddes AJ. Use of graphics workstations to illustrate protein and nucleic acid structure: A description of three modeling experiments carried out by second-year undergraduates. Biochem Educ. 1996; 24(1): 32-35.

4. Das N, Sinha S. Problem-oriented small-group discussion in the teaching of biochemistry laboratory practical. Biochem Educ. 2000; 28(3): 154-155.

5. Latruffe N, Hassell SJ. Peroxisomes: Biochemistry, molecular biology and genetic diseases- a video programme for teaching students. Biochem Educ. 2000; 28(3): 136-138.

6. Weldon SL, Jones MA. Kinemages as a visualization tool for biochemistry classes. Biochem Educ. 1995; 23(4): 208-212.

7. Weiner SW, Cerpovicz PF, Dixon DW, Harden DB, Hobbs DS, et al. RasMol and Mage in the undergraduate biochemistry curriculum. J Chem Educ. 2000; 77(3): 401-406.

8. Richardson DC, Richardson JS. Teaching Molecular 3-D Literacy. Biochem Mol Bio Educ. 2002; 30(1): 21-21.

9. Tasi CS. Microcomputer application in Biochemistry. J Chem Educ. 2000; 77(2): 219-221.

10. Sansom CE, Smith CA. Computer applications in bimolecular sciences. Part 2: bioinformatics and genome project. Biochem Educ. 2000: 28(3): 127-131.

11. Smith C. Problem-based learning. Biochem Educ. 2000; 28(3): 143.

12. Parslow GR. Computer-based learning. Biochem Educ. 2000; 28(3): 156.

13. Jenkins RO. Biotechnology Education. Biochem Educ 2000; 28(3): 160.

14. Soltani S, Abolhasani H, Zarghi A, Jouyban A. QSAR analysis of diaryl COX-2 inhibitors: Comparison of

feature selection and train-test data selection methods. Eur J Med Chem. 2010; 45(7): 2753-2760.

15. Qujeq D. A simple method for instructing protein structure for medical students: A case review. J Med Educ. 2002; 2(1): 48-51.