Teaching Efficiency
Ефективност на обучението

SIMULATION OF THE FATTY ACID SYNTHASE COMPLEX MECHANISM OF ACTION

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Abstract. One of the most complicated subjects to our students is the fatty acid synthase (FAS) complex. The objective of this article is to make the lecture of fatty acid synthesis enjoyable and understandable through mimicking the action of the fatty acid synthase complex by our students.Fatty acid synthase mechanism of action is mimicked by two students using highlighter markers with or without caps.The sketch was evaluated by simple questionnaire. 77.5% of the students agreed that the sketch was very useful and helped them to better understand the FAS structure and mechanism of action while 22.5% of the students were not happy by the sketch.Mimickingtheaction of complex biological molecules is an effective tool to facilitate better understanding of biochemistry.A lot of efforts should be done to make the biochemistry an interesting science for the students.

Keywords: teaching biochemistry, fatty acid synthase, malonyl CoA, sketching method

Introduction

The biochemistry department of the faculty of medicine of International University of Africa is a central department which teaches biochemistry courses to undergraduate students of the faculties of medicine, dentistry, pharmacy, laboratory technology, nursing and science.The department philosophy of teaching is to use different methods in teaching so as to facilitate better understanding of biochemistry. The different teaching methods are lectures, practical sessions, tutorials;problem based learning, guided assignment writing, seminars and guided research proposal writing, research implementation and research report writing. Although of our efforts to conduct the biochemistry curriculum using different methods, our students feel that the biochemistry is a tough, boring and irrelevant subject. Their feeling is reflected in their performance in the examinations, mostly, 30% of our students fail in their final exams.

This feeling of our students is not seen only in our faculty alone, but is shared by other students from local, regional or international faculties. This feeling is mostly due to the fact the biochemistry involves an overload information .e.g. new scientific terms,

names of enzymes and the metabolic pathways (Novelli&Fernandes, 2007). To make the biochemistry more interesting, the large biochemistry community introduced different teaching methods including, lectures (Novelli& Fernandez, 2007), practical sessions in different ways (Reiter et al., 2000; Sweney et al., 2004; Bartho et al., 2012), problem based learning (Smith, 2002; Novelli&Fernandes, 2007; Se et al., 2008), usage of computer and internet resources (Tonukari, 2006), usage of movies to facilitate better understand of enzyme mechanism of action (Cheung & Cramer, 2012) and research which facilitate self-learning and problem solving (Prober & Heath, 2012).

In order to solve the problems of medical students in understanding the biochemistry, the department decided to introduce other teaching methods so as to remove the feeling of irrelativeness and to change the biochemistry into easy and interesting subject. One of the approved methods is to portray the mechanism of action of complex molecules through simple sketches using some of the class students as actors.

The department of biochemistry is facing shortage in staff and teaching resources. There is heavy brain drain towards gulf countries because of the very high salaries compared to the local ones. Regarding the teaching resources, we have decided to use the available resources in order to meet the teaching objectives and to overcome the shortage problems; for example and instate of using biochemistry models we are using markers and high lighters and their caps as enzyme substrates, students as polypeptides and two threads with different colors as DNA molecule.

Fatty acid synthesis

Fatty acid synthesis is an active anabolic pathway during fed state. Fatty acid synthesis is active in the cytoplasm of the liver, kidney, brain, lung, mammary gland and adipose tissues (Murray et al., 2009). Two enzymes are responsible for catalyzing the fatty acid synthesis, acetyl CoA carboxylase and fatty acid synthase.

The acetyl CoA carboxylase converts acetyle CoA and biocarbonate to malonyl CoA, it needs biotin as cofactor. The fatty acid synthase uses Acetyl CoA and Malonyl CoA as substrates and it needs NADPH as cofactor. Regarding the structure of the fatty acid synthase, it is composed of two poly peptide chains (two structural domains). Each poly peptide chain contain the activity of seven enzymes and two sites, one for malonyl CoA binding and the other for acetyl CoA or Acyl CoA binding. The fatty acid synthase complex is a bifunctional enzyme; it synthesizes two fatty acids simultaneously (FAS is composed of two functional domains).

The seven enzymes are ketoacyl synthase, acetyl transacylase, malonyltransacylase, hydratase, enoylreductase, ketoacylreductase and thioesterase. However, each poly peptide contains an acyl carrier protein moiety (ACP, the active form of vitamin B5) (Murray et al., 2009).

Mechanism of action of FAS

At the level of the functional domain, the malonyl groups ofmalonyl CoA moleculesare transferred to the ACP moietiesof the fatty acid synthase by the action of the malonyltransacylase and CoA molecules are released.On the other hand two Acetyl CoA molecules react withketoacyl synthase enzymes of the FAS by the action of acetyl transacylase, acetyl groups are bound to theketoacyl synthase enzymes and CoA moieties arereleased. The acetyl moiety is transferred to the ACP and is bound to the malonyl group forming acetoacetyl and releasing carbon dioxide by the action of ketoacyl synthase. The ketoacyl group is reduced and dehydrated by two NADP linked reductases and one dehydratase forming acyl group. The acyl group is transferred from the ACP and bound to the ketoacyl synthase and another malonyl group binds the ACP. The process is repeated till free fatty acid is released by the action of thioesterase enzyme (Murray et al., 2009).

Material and methods

The structural domain of the fatty acid synthase is portrayed by two students (Fig1). The right hand of each student represented the site of malonyl binding while the left hands represent the site of acetyl binding. The students stand facing each other. The right hand of one student and the left hand of the other are considered as the functional domain of the fatty acid synthase.

A green highlighter cap was used to represent the CoA and an orange cap was used as carbon dioxide (Fig.2). The malonyl CoA was represented by a highlighter with two caps, green and orange while a highlighter with orange cap only was used to act as malonyl group (Fig.3). A highlighter with green cap was considered as the acetyl CoA molecule and a highlighter without cap represented the acetyl moiety (Fig.4).

The functional domain of FAS is represented by the left hand of one student carrying acetyl group and the right hand of the other student carrying malonyl group (Fig.5).

To mimic the functional unit of the fatty acid synthase, one student hold a capped highlighter (malonyl) at his right hand and released the green cap (CoA) and the other student hold a de capped highlighter (acetyl) at his left hand and also released the green cap (CoA).

The student with the de capped highlighter on his left hand transferred it to the capped highlighter on the right hand of the second student, released the orange cap (carbon dioxide) from the capped highlighter and hold the two de capped highlighter together (acetoacetyl).

The students were told that after the two highlighters are joined together three reactions occur; reduction, dehydration and reduction and after the three reactions the keto acyle group is converted to acyl group with four carbons (two highlighter). The two joined highlighters are transferred from the right hand of the second student to the left hand of

the first student and the second student hold another capped highlighter (malonyl) releasing a green cap (CoA). The two joined highlighters are transferred from the left hand of the first student to the malonyl moiety on the right hand of the second student and the orange cap is released. The students were told that, at this level, the three cyclic reactions occur again (reduction, dehydration and reduction) and the result is the formation of another acyl group with six carbons (three highlighters). The joined three highlighters are transferred from the right hand of the second student to the left hand of the first student, another caped highlighter is bound to the right hand of the second student and the three highlighters are transferred from the left hand of the first student to the right hand of the second student forming a molecule with four highlighters (eight carbons).

The students were told that the process is repeated, in the two functional domains of the fatty acid synthase, for several times in order to release two mature fatty acids simultaneously.

Evaluation of the new teaching method

The new teaching method was evaluated by distributing a simple questionnaire to the students. The mimicking of the FAS structure and mechanism of action by my colleagues using highlighters and their caps facilitated better understanding of FAS: a- I strongly agree; b-I agree; c- I disagree.

Results and discussion

Previously the lecture of fatty acid synthesis was very boring to our students and, mostly, at the end of the lecture half of the class will be out the lecture room. After conducting the lecture by the new method all the students clapped and shout by one voice (interesting). They named the two students as fatty acid synthase one and two.

However, the total number of the students attending the lecture was 102 students and their opinions about the lecture was as follows: 23 (22.5%) of the students disagreed, 32 (31.4%) agreed and 47 (46.1%) strongly agreed that the sketch facilitated better understanding of the structure and mechanism of action of the fatty acid synthase (Table 1).

Table.1. Students and their opinions about the FAS sketch

Total number	Strongly agree students	Agree students	Disagree students
102	47	32	23
Percentage %	46.1	31.4	22.5

From the above table it is clear that the sketch facilitated better understanding of the structure and mechanism of action of FAS for the majority of the students 79 (77.5%).

Conclusion

It was clear that mimicking the structure and mechanism of action of complex molecules by the students is an effective teaching method for biochemistry.

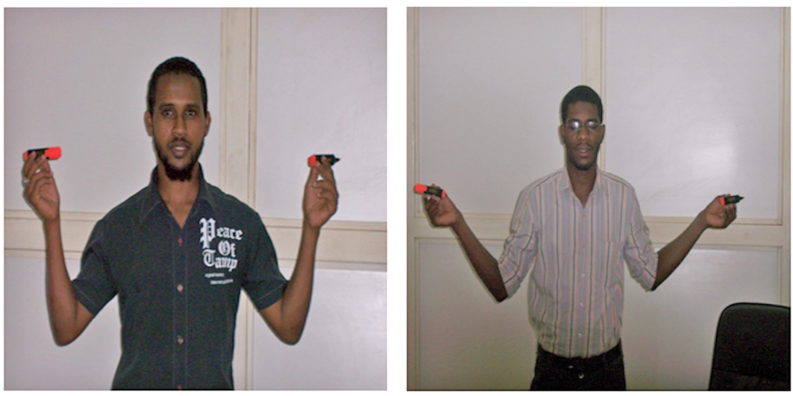

Fig.1. Structural domains of fatty acid synthase
The two polypeptide chains of the fatty acid synthase complex are mimicked by two students carrying highlighters in their hands. A malonyl group on the right hand (a highlighter with an orange cap) and an acetyl group on the left hand (a highlighter without cap).

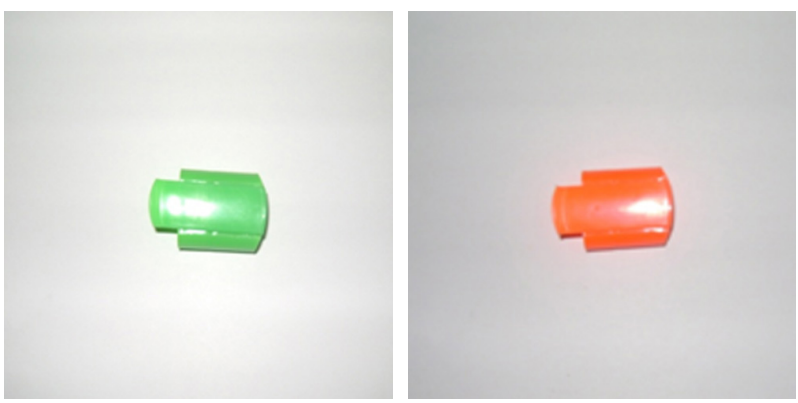

Fig. 2. Coenzyme A (CoA) and carbon dioxide
The green highlighter cap was used to act as Coenzyme A (CoA) and the orange cap was used as carbon dioxide.

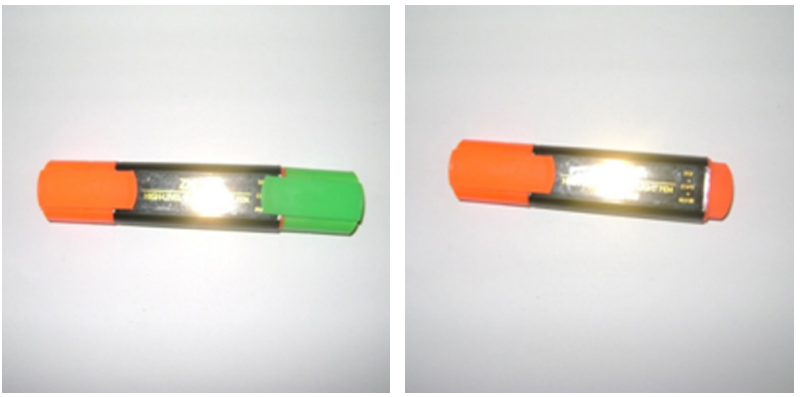

Fig. 3. Malonyl CoA and malonyl moieties
A highlighter with a green and an orange cap was used as Malonyl CoA ($OOC\text{-}CH_2\text{-}CO\text{-}SCoA$) and a highlighter with an orange cap only ($OOC\text{-}CH_2\text{-}CO$) was used for malonyl group.

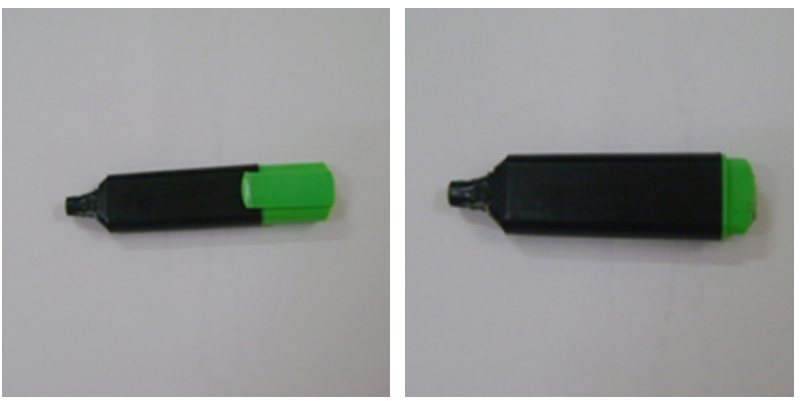

Fig. 4. Acetyl CoA and acetyl groups
The Acetyl CoA was mimicked by a highlighter with a green cap ($CH_3\text{-}CO\text{-}SCoA$) and the highlighter without a cap represented the acetyl group ($CH_3\text{-}CO$).

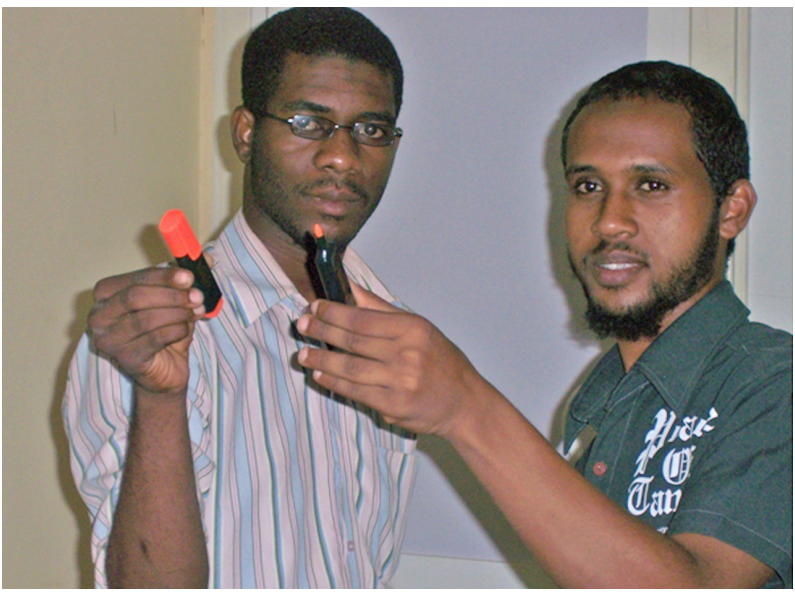

Fig. 5. The functional domain of the FAS
The functional domain of the FAS was mimicked by the right hand of one student (polypeptide one) and the left hand of the other student (polypeptide two). One was carrying a molonyl group (a highlighter with the orange cap) and the second was carrying an acetyl group (a highlighter without cap).

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