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Online Applied Problem-Based Learning to Determine the Shelf Life of an on-Site Solution of Refrigerated Drug

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Abstract

A problem-based online learning (PBe-L) teaching sequence was designed for calculating the shelf life (expiration date) of an on-site solution of refrigerated drug as part of activities of a Pharmaceutical Physical Chemistry course of Pharmacy major at FES Cuautitlán UNAM in Mexico. The teacher presents students the problem, a group collaborative activity is carried out to search for information in PBL cycles. Students are then shown a virtual experiment that includes experimental results. Another group collaborative activity is carried out for the search of information, for the procedural analysis of the results. Applying knowledge and understanding of the topics of chemical kinetics, temperature effect on the rate of chemical reactions and drug degradation reactions, etc., students solve the problem. Hake's factor was determined for the conceptual gain. A Likert-type satisfaction survey was conducted and compared to the results of a group that was applied to the PBL strategy in person. At the end of the sequence students achieved recognition, comprehension and application learnings and conceptual gain was high. Allowing an integration of its cognitive framework of kinetics topics.

Keywords:
PBL
Expiration date
Kinectics
Temperature.

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1. Introduction

The teaching learning of Pharmaceutical Physical Chemistry for the career of Pharmacy and related careers, at the Faculty of Cuautitlán Higher Studies of the National Autonomous University of Mexico UNAM, is taught in an experimental theoretical way, usually with exercises and practices but lacks a real link with the pharmaceutical area that generates high rates of failed. Various teaching strategies have been used to stimulate interest and promote meaningful learning in students.

For the improvement of the learning teaching process, a lot of teaching strategies have been designed, including problem-based learning (PBL) (Woods, 2014). PBL is the learning that results from the entertainment process or solution of a problem (Obaya, Vargas-Rodríguez, Lima-Vargas, & Vargas-Rodríguez,

2018). PBL offers students an obvious answer to questions: Why do we have to learn this information? And what I do in school have something to do with the real world? (López, 2008).

PBL is a teaching method that substantially increases students' motivation, since by its dynamics it makes students active subjects of the learning teaching process (García, 2008). The student is also the center of this process and working with this method requires teamwork of non-individual students (Williams, 2016); (Obaya, Vargas-Rodríguez, Giammatteo, & Ruiz Solórzano, 2019).

PBL consists of the approach of a problem situation; where its construction, analysis and/or solution are the central focus of experience, and where teaching is to deliberately promote the development of the process of inquiry and resolution of problems. The various modalities adopted today by the PBL are elements of the constructivist theories of learning, which highlight the need for students to research or intervene in their environment and build for themselves meaningful learnings (Obaya, Vargas, & Delgadillo, 2011). PBL is based on the principle of using problems of everyday life or professional exercise as a starting point for the acquisition and integration of new knowledge.

The appropriate "good problems" to work with in the classroom through PBL cycles are those that are defined as open or unstructured, ambiguous, likely to change and to propose various solutions (Edens, 2000). PBL has been applied to the teaching of the chemical sciences Bodner and Bhattacharyya, (2005); Hicks and Bevsek (2012); Flynn and Biggs (2012); Moutinho, Torres, Fernandes, and Vasconcelos (2015); Cowden and Santiago (2016) and the teaching of Physical Chemistry Ramos—Mejia and Palacios-Alquisira, (2007); Da Silva, Vieira, and Ferreira (2013); Gurses, Dogar, and Geyik (2015); Turcio-Ortega and Palacios-Alquisira (2015); Fernández and Aguado (2017); Obaya et al. (2018). PBL has been successfully applied in various pharmacy subjects, for example, with an industry-based focus on drug administration courses (Hussain, Sahudin, Samah, & Anuar, 2019) in chemistry courses for teaching functional groups (Perez-Rivero, Obaya Valdivia, Giamatteo, Montaño-Osorio, & Vargas-Rodríguez, 2019).

On the other hand, with the current use of tablets and personal computers pharmacy students from some universities prefer a combination of classroom teaching and online learning (Hamilton et al., 2020).

In this work, the application of a teaching sequence of learning based on online problems is presented, to improve learning of the topic of rate reaction effect in a course of Pharmaceutical Physical Chemistry.

2. Methodology

The teaching sequence was applied in a group of 22 students of Pharmaceutical Physical Chemistry, part of the Pharmacy major of the Faculty of Higher Studies Cuautitlán of the National Autonomous University of Mexico UNAM. The ages of the students ranged from 20-22 years. Previously, a video was made with the simulation of an experiment (Vargas-Rodríguez et al., 2016). Also, an evaluation tool was designed, which was uploaded to the Google forms platform. The class was conducted via Video Platform and Audio Online Conferencing Zoom.

Once students were connected to the platform, the objective of the class, the way of work was indicated and the link of a Google form (pretest) was sent to the Zoom chat to evaluate the previous knowledge, it was resolved individually in a maximum time of 20 minutes Annex 1. Subsequently, in a PowerPoint presentation, the problem was presented: *What is the shelf life (expiration date) of an extemporaneous preparation of aspirin stored in refrigeration*? From this, a group collaborative activity was carried out for the search for information, in PBL cycles, the teacher only served as a guide to this process. Students were then presented with the "virtual experiment" of hydrolysis of aspirin (AAS) at 40, 50 and 60 ^{0}C respectively in which the pH results based on time were appearing in the digital presentation "in real time", made in accordance with the methodology published by Vargas-Rodríguez. et al. (2017). Also, it was analyzed what type of waste would be generated if the experiment had been carried out in the laboratory and the possible treatment of waste (Vargas-Rodríguez et al., 2016). From observations and experimental results, questions again arose, focused on solving the initial problem, for which another group collaborative activity was carried out to search for information through PBL cycles. With enough information to solve the problem, students determined from pH, the remaining NaOH concentration, the reaction order of the degradation of AAS, at each temperature. Using the Arrhenius equation and trough interpolation, they determined the count of rate of the cooling temperature and the shelf life of the extemporaneous preparation. It should be noted that, the teacher asked several students to share their screen to follow up on this procedural activity. To close the class, students were asked if they liked the class. Subsequently, students were asked to answer a post-post on the Google platform, in a maximum time of 20 minutes Annex 1 and answer a Likert satisfaction survey. Finally, the students sent the presentation of their results to the teacher. To evaluate the learnings achieved, the results of the pretest and postest were compared and the normalized factor or gain (g) of Hake was determined according to Equation 1 (Hake, 1998) where g, is reported as the ratio between the results of % of correct postest and pretest responses.

$$g = \frac{postest\% - pretest\%}{100\% - pretest\%} \quad (1)$$

Finally, in order to know the opinion of the students regarding the PBL strategy applied in the resolution of the problem, a questionnaire with Likert scale was applied, to determine the degree of usefulness and their satisfaction of the teaching strategy used to study the issue of temperature effect on the speed of reaction. The scale of the instrument was: 1. Very disagreed, 2. Disagreement, 3. Indifferent, 4. Agreement and 5. Very agreed. Students resolved it anonymously Table 1, was also done using a Google form.

Table-1. Assessment of the degree of usefulness and satisfaction of the PBL applied online.

1. Do you think the online strategy that motivates problem solving?
2. Does the online strategy make it easier to understand the issue of temperature effect on reaction speed?
3. Do you find the online data processing strategy useful?
4. Do you consider it to facilitate teamwork?
5. Do you consider yourself satisfied with the online teaching strategy used for determining the lifetime?

3. Results and Discussion

In order to achieve meaningful learnings of the issue of temperature effect on the rate of chemical reactions, an online PBL didactic strategy was applied. After presenting the problem, a collaborative group activity was carried out for the search for information, in PBL cycles, where new questions such as those shown in Table 2. It also shows some of the questions that arose during experimental activity and in collaborative activities, for problem solving (PBL cycles).

Table-2. Stages of online PBL.

1	The problem arises to students.
2	Collaborative activity for the search for information (PBL cycle generator).
3	Experimental collaborative activity for information gathering.
4	Collaborative activities for treatment and disposal of waste (environmental problems).
5	Observations and experimental results.
6	Conceptual and procedural collaborative activities (through PBL cycles).
7	Presentation of results and conclusions (argumentative, characteristic of PBL).

Figure 1 presents the results of the pretest and the applied postest, to determine the improvement of the teaching and learning on the topic of temperature effect in the rate of chemical reactions. It should be noted that items one to seven are related to the topic of chemical kinetics, from eight to 13 to fundamentals of the effect of temperature on the rapidity of chemical reactions and from 14 to 20, to the subject effect of temperature on the degradation of drugs and medicinal products. Also, the items were classified based on Bloom's taxonomy (Marzano, 2001) as shown in Table 3, being classified into three levels, level one (N1) recognition, level two (N2) comprehension and level three (N3) application. Based on this classification, item 20 can be analyzed in N3, the topic of fundamentals of the temperature effect on the rate of chemical reactions or on the subject of drug and drug degradation. As you can see, the learnings of the three topics improved after the implementation of the strategy.

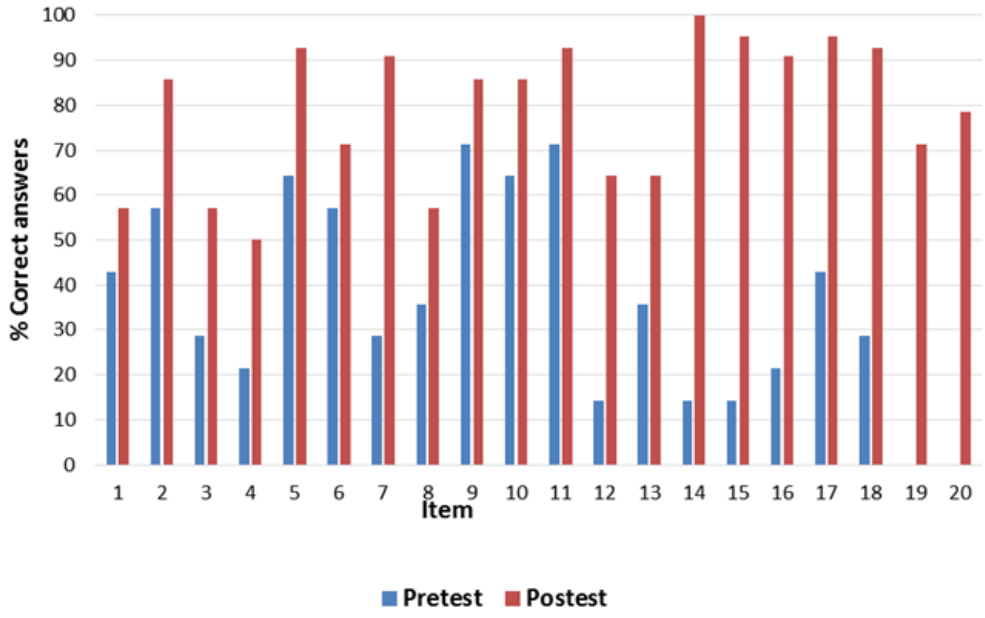

Figure-1. Pretest and postest results applied to the group.

Table-3. Classification of items based on bloom taxonomy (Marzano, 2001).

Subject	Taxonomic level	Learning indicator	Item
Chemical Kinetics	1	Recognizes terms and methods used in chemical kinetics	1-2
	2	Understands the concepts that define chemical kinetics	3-6
	3	Applies your knowledge of chemical kinetics to determine a drug's half-life	7
Basics of the temperature effect on the speed of the reaction	1	Recognizes the parameters that are determined by the Arrhenius equation and collision theory	8-11
	2	Understands the basis of the effect of temperature on the speed of the reaction	12-13
	3	Applies your knowledge of collision theory and transition status to determine the shelf life date of an out-of-time formulation.	20
Drug degradation and temperature effect on rapid degradation	1	Recognizes out-of-time formulations as well as the structure of the AAS	14-15
	2	Understands the importance of functional groups in the structure of drugs and what produces its breakdown	16-19
	3	He applies his knowledge of chemical kinetics, temperature effect on the rapid reaction and degradation of drugs, to determine the shelf life of an extemporaneous formulation.	20

To analyze, the difference in learnings between pretest and postest, Hake's standardized gain was determined Figure 2. This factor is reported as a number between zero and one. It is observed that g, has mean values ($0.3 \leq g \geq 0.7$) for most of the responses in the topic of chemical kinetics, with an average of g-0.56, in both the answers of the fundamentals of the topic of temperature effect on the speed of reaction with an average factor of g x 0.57 and high values ($> 0.7 - 1.0$),for the topic of drug grading and temperature effect on the speed of degradation, these results are characteristic of active learnings such as the PBL applied in this strategy (Hake, 1998).

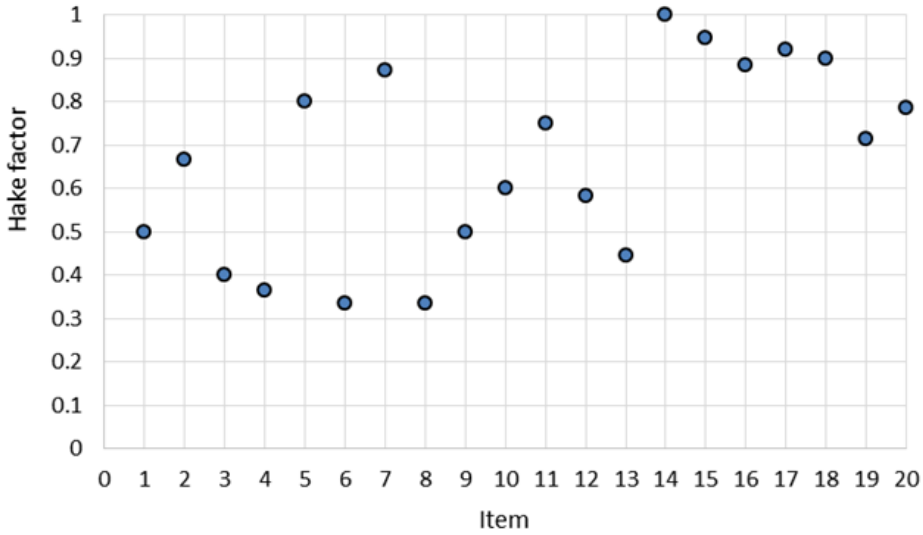

Figure-2. Hake factor vs Item.

Also, students were asked if and what they liked about the problem and the answers were in general, that the problem used a drug, in this case the AAS, the use of out-of-time preparations, see the degradation of the drug, from the point of view of the molecular structure and in particular the functional groups, integrate concepts such as pH and balance with the speed of reaction, and in particular its application at the expiration date.

Finally, the satisfaction survey obtained from the PBL online Figure 3, was compared with that obtained in another group of Pharmaceutical Physical Chemistry, to which the face-to-face PBL was applied and which was developed in the laboratory, where the survey questions were adapted to the presence PBL Table 4. The

results revealed that 72.7% of students agreed or very much agree on that this online activity motivates the resolution of the problem, 63.63% indicated that it facilitates the understanding of the topic, 50% consider useful to the online strategy for data processing (which was carried out in Excel), 50% consider that it facilitates group work. However, 86% were satisfied with online activity to determine the shelf life or expiration date of a drug. As for the results of the group to which the face-to-face PBL was applied, they are shown in Figure 4; 92.7% of students agreed or very much agree on that this online activity motivates laboratory work to solve the problem, (e) 100% replied that it facilitates understanding of the topic, 10 0% consider useful to the face-to-face PBL strategy for data processing (which was performed in Excel), 92.7% consider that it facilitates group work and the same percentage is considered satisfied with the strategy to determine the shelf life date or expiration date of a drug. It is noted that motivation, understanding of the subject, usefulness for data processing, ease of working as a group or equipment and satisfaction are always lower in the online PBL than in the face-to-face PBL, It should be also noted that in the question Do you consider useful the strategy for data processing?, in the face-to-face PBL is 100% and online 50%, it is attributed that in the laboratory were working on teams of 5 students and online the whole group, which prevented adequate follow-up for the processing of data in the spreadsheets by the teacher to each student or group of students. Similar results were obtained by replying: Do you consider that the strategy facilitates group/teamwork? In the case of face-to-face PBL was 92% and in the online PBL of 50%, this difference is probably due to the fact that in the face-to-face PBL the students performed laboratory work in equipment, while, in the online PBL although the sequence was done in a group form, each student worked on his personal computer, interacted in less proportion with his peers, intermediate results (62.5%), have been obtained with the PBL for teaching and learning the subject of rapid reaction applied in person in the classroom (Obaya. et al., 2018). Finally, in terms of the satisfaction of the teaching strategy was 72.7%, 92.7% and 85.7%, for the online PBL strategy, face-to-face ABP in the laboratory and face-to-face PBL in the classroom respectively, indicating that students are slightly more satisfied with face-to-face PBL than online (Stern, 2004).

Table-4. Assessment of the degree of usefulness and satisfaction of face-to-face PBL.

1. Do you think the strategy motivates the laboratory work for solving the problem?
2. Does the strategy make it easier to understand the issue of temperature effect on reaction rate?
3. Do you find the strategy for processing laboratory data useful?
3. Do you consider it easier to work as a team?
5. Do you consider yourself satisfied with the teaching strategy used for determining the shelf life?

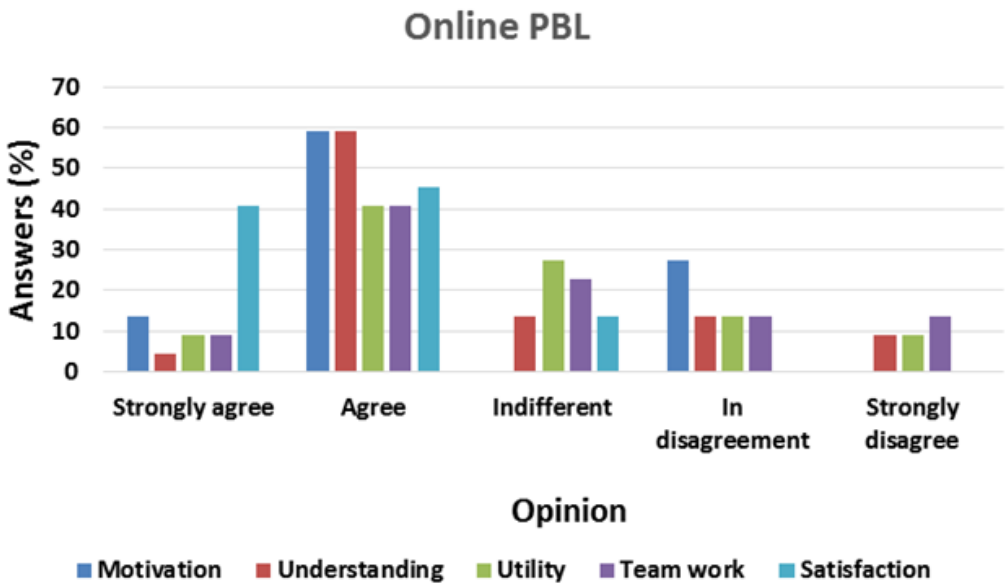

Figure-3. Likert survey results (online PBL).

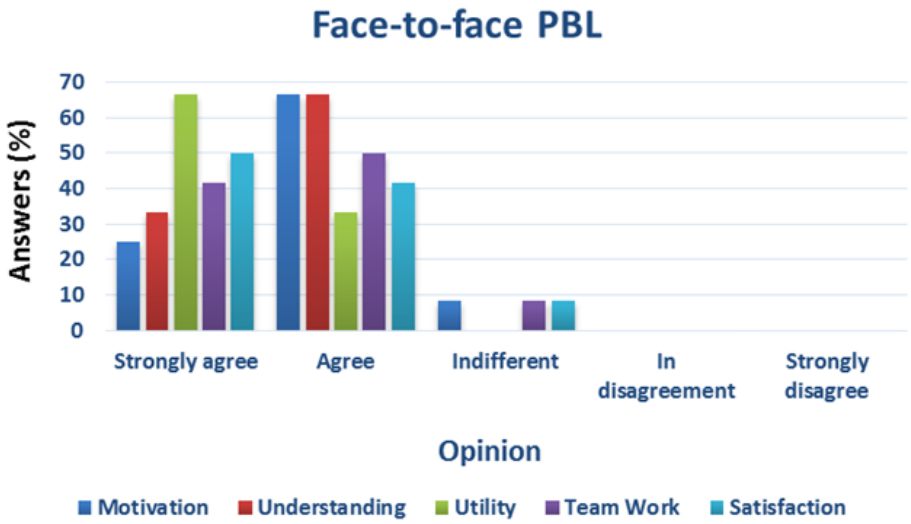

Figure-4. Likert survey results (Face-to-face PBL).

4. Conclusions

After applying and evaluating a teaching sequence based on Online Problem-Based Learning (e-PBL) to improve temperature effect topic learnings on the speed of reaction in a Pharmaceutical Physical Chemistry course and resolve the question: What is the shelf life (expiration date) of an out-of-time preparation of acetylsalicylic acid stored in refrigeration?, it is concluded that, according to Bloom's taxonomy, students recognized, understood and applied the knowledge acquired from the subject and that Hake's standardized gain was high, indicating active student participation, despite the problem that students are not accustomed to online classes. In addition, the student's comments on the problem were very positive, as they were pleased to know that it is an out-of-time preparation, to understand the main degradation reactions of a drug, to identify which functional groups in the drugs are susceptible to hydrolysis, to understand that it is an accelerated stability study and to understand the meaning of an expired drug from the point of view of chemical kinetics. . As for the Likert-type satisfaction survey, 50% of students consider the online strategy for data processing useful and that it facilitates group work, 63.63% consider that the activity facilitates the understanding of the topic, 72.7% of students agreed or very much agreed that this online activity motivates the resolution of the problem and 86% were satisfied with the PBL activity online. Finally, students are slightly less satisfied with e-ABP than with face-to-face PBL. Problem-based online learning is an appropriate method for teaching Pharmaceutical Physical Chemistry. This may be due to several factors, including the location of the semester of the subject (5th semester) and transversality of the subject in the curriculum, allowing an integration of its cognitive framework.

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Annex-1. Google Questionnaire.

1. ¿Which units presents the zero-order rate constant?	a) Ms^{-1} b) s^{-1} c) $M^{-1}\ s^{-1}$ d) $M^{-2}\ s^{-2}$
2. When using the graphical integral method to determine the reaction order of a second-order reaction. What is plot?	**a**) 1/(Ao-x) ^2 vs t b) 1/(Ao-x) vs t c) (Ao-x) vs t d) ln (Ao-x) vs t
3 Identify the kinetic equation that presents the following reaction $2A + 3B \rightarrow C + 2D$	a) $r = -\frac{d[A]}{dt} = -\frac{d[B]}{dt} = +\frac{[C]}{dt} = +\frac{[D]}{dt}$ b) $r = -\frac{1}{2}\frac{d[A]}{dt} = -\frac{1}{3}\frac{d[B]}{dt} = +\frac{[C]}{dt} = +\frac{1}{2}\frac{[D]}{dt}$ c) $r = +\frac{1}{2}\frac{d[A]}{dt} = +\frac{1}{3}\frac{d[B]}{dt} = +\frac{1}{1}\frac{[C]}{dt} = +\frac{1}{2}\frac{[D]}{dt}$ d) $r = -\frac{1}{2}\frac{d[A]}{dt} = -\frac{1}{3}\frac{d[B]}{dt} = -\frac{1}{1}\frac{[C]}{dt} = \frac{1}{2}\frac{[D]}{dt}$
4. Identify the law of rate for the breakdown of a drug A that in presence B, degrades according to the following reaction: $A + 2B \rightarrow C + D$	a) $r = k\,[A]^1[B]^2$ b) $r = k\,[A]^2[B]^1$ c) $r = k\,[A]^{\alpha}[B]^{\beta}$ d) $r = k\,[C]^1[B]^1$

5.What is the partial reaction order with respect to reagent A, reagent B and global is, for the next rate equation? $r = k\,[A]^2[B]^1$	a) 2, 1 y 3 b) 1, 2 y 3 c) 3, 2 y 1 d) 1, 1 y 2.
6.It has been observed that a reaction, by increasing the concentration of A and B the speed of reaction increases, so it can be said that the best representation for the speed of reaction is:	a) $r = k\,[A]^0[B]^1$ b) $r = k\,[A]^2[B]^{1/3}$ c) $r = k\,[C]^{1/2}[B]^1$ d) $r = k\,[A]^1[B]^2$
7. ¿What is the half-life of a drug that, at 25oC, is broken down with a kinetics of the first order? Constant of speed k=4.8135 x 10^{-4} s^{-1}	a) 4 h b) 8 h c) 24 h d) 2 h
8. What parameters are determined by the Arrhenius equation?	a) Activation power, activation Gibbs power, and Internal activation power. b) Frequency factor, Activation energy and activation enthalpy. c) Frequency factor and Activation energy d) Frequency factor, activation energy and activation entropy
9. ¿What thermodynamic activation properties can be determined, with the transition state theory and the Eyring equation?	a) Activation energy, activation Gibbs power and internal activation energy, activation enthalpy and frequency factor. b) Activation entropy, activation energy, activation enthalpy, Internal activation energy, activation enthalpy. c) Gibbs Activation Energy, Activation Entropy, Activation Enthalpy, Internal Activation Energy, Activation Enthalpy, Frecuency Factor. d) Frequency factor, activation energy and activation enthalpy
10. Is the activation energy for a reaction to occur?	a) It's the minimum energy for you to initiate a chemical reaction b) It is the minimum energy for a chemical reaction. c) It is the maximum energy for a chemical reaction to be performed. d) It is the maximum energy for it to initiate a chemical reaction.
11.Consider that a drug A, is broken down in the presence of B, to give C + D, at constant temperature. $A + B \rightarrow C + D$ Based on collision theory, what is required for drug breakdown to occur?	a) A sufficient activation energy that allows the formation of active species of A and B, which frequently collide with an adequate orientation that allows the rupture and /or formation of new links. b) A sufficient activation energy to allow the formation of active species of A and B, which frequently collide. c) Suitablely oriented shocks that can break the chemical bonds present in molecules A and B and in turn, can contribute to the formation of new bonds. d) No energy is needed, molecules collide naturally.
12.Assuming the same reaction from the previous point, by increasing the temperature, the most likely thing that can happen is:	a) That the rapidity constant increases, due to the increase in the kinetic energy of molecules, which produces more shocks between the active forms of A and B. b) That the rapid constant increases, due to the increase in activation energy. c) That the rapidity constant decreases by the increase in activation energy. d) That the rapid constant of not being changed, since, by not increasing the concentration of the reagents, the number of collisions will not be increased.
13.If the temperature drops, it is likely that	a) That the rapidity constant decreases, due to the decrease in

	the kinetic energy of the molecules, which produces fewer collisions between the active forms of A and B. b) That the rapidity constant decreases, due to the decrease in activation energy. c) May the rapid constant increase by the decrease in activation energy. d) That the rapid constant of not being changed, since, by not increasing the concentration of the reagents, the number of collisions will not be increased.
14.¿What is the chemical structure of the AAS?	
15. ¿What is an out-of-time pharmaceutical preparation?	
16. ¿Explain, the main drug degradation reactions?	
17. Identify which functional groups in the drugs are susceptible to hydrolysis	
18. Explain which is an accelerated stability study.	
19.Explain the meaning of an expired drug from the point of view of chemical kinetics.	
20. Determine the shelf life of an extemporaneous formulation of a drug that, at 25ºC, is broken down with a first-order kinetics with a constant of speed k=2.107x10-3 min-1	a) 200 min b) 150 min c) 5 min d) 50 min