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CLINIC AND SURGERY

Three-dimensional models for teaching the mechanisms of action of phenothiazines and butyrophenones in veterinary medicine

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Modelos tridimensionais para o ensino dos mecanismos de ação das fenotiazinas e butirofenonas na medicina veterinária

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ABSTRACT: Phenothiazines (FNZ) and butyrophenones (BUT) are commonly used as sedatives and tranquilizers in the field of veterinary anesthesia. The greatest difficulties students face when studying the mechanisms of action of these drugs involve the spatial perception and configuration of these molecules. Therefore, the present study to evaluated the use of three-dimensional (3D) models representing the mechanisms of action of FNZ and BUT as tools in the teaching and learning of pharmacology and anesthesiology in veterinary medicine. Thirty-eight students participated in the study and were divided into two groups: the 3D group (G3D), comprising students who studied using 3D models, and the Control Group (CG), in which students studied the mechanisms of action using flat diagrams. Pre- and post-tests were administered to assess students' level of knowledge regarding the mechanism of action and functions of FNZ-BUT in the body. Only the G3D group showed significant improvements between the pre- and post-tests in terms of understanding of mechanism of action (P = 0.010) and function (P = 0.001). The average gain in marks was marked for the G3D students, with a significant difference in the mechanism of action (P = 0.043) compared to CG. These results indicated that the use of 3D models is more efficient than the use of flat diagrams in promoting learning about FNZ-BUT, particularly regarding their mechanism of action. Tactile experiences with physical objects are believed to stimulate students' concentration, interest, and learning about a subject.
Key words: education, anesthesiology, pre-anesthetic medication, learning.

Modelos tridimensionais para o ensino dos mecanismos de ação das fenotiazinas e butirofenonas na medicina veterinária

RESUMO: As fenotiazinas (FNZ) e as butirofenonas (BUT) são comumente utilizadas como sedativos e tranquilizantes no campo da anestesiologia veterinária. As maiores dificuldades enfrentadas pelos estudantes ao estudar os mecanismos de ação desses fármacos envolvem a percepção espacial e a configuração dessas moléculas. Neste sentido, o presente estudo teve como objetivo avaliar o uso de modelos tridimensionais (3D) representando os mecanismos de ação das FNZ e BUT como ferramentas no ensino e aprendizagem de farmacologia e anestesiologia na medicina veterinária. Para avaliar o uso de modelos tridimensionais, participaram do estudo trinta e oito estudantes, divididos em dois grupos: o grupo 3D (G3D), composto por alunos que estudaram utilizando modelos tridimensionais, e o Grupo Controle (GC), no qual os alunos estudaram os mecanismos de ação por meio de diagramas bidimensionais. Além disso, foram aplicados testes antes (pré-teste) e após (pós-teste) a intervenção para avaliar o nível de conhecimento dos alunos sobre o mecanismo de ação e as funções das FNZ-BUT no organismo. Somente o grupo G3D apresentou melhorias significativas entre o pré e o pós-teste, tanto na compreensão do mecanismo de ação (P = 0,010) quanto da função (P = 0,001). O ganho médio nas notas foi expressivo para os alunos do G3D, com diferença significativa no quesito mecanismo de ação (P = 0,043) em comparação ao GC. Esses resultados indicam que o uso de modelos tridimensionais é mais eficiente do que o uso de diagramas bidimensionais na promoção da aprendizagem sobre FNZ-BUT, especialmente no que diz respeito ao seu mecanismo de ação. Portanto, acredita-se que experiências táteis com objetos físicos estimulem a concentração, o interesse e a aprendizagem dos estudantes sobre o tema.
Palavras-chave: educação, anestesiologia, medicação pré-anestésica, aprendizado.

INTRODUCTION

The use of sedatives is an important aspect of veterinary clinical practice, as it reduces the animal's physical and psychological stress, ensuring that safer procedures can be carried out, while also considering the patient's well-being FISCHER & CLARK-PRICE (2015). These drugs, which include

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phenothiazines (FNZ) and butyrophenones (BUT), BORGES et al. (2022), reduce anxiety and facilitate responses to external stimuli.

The greatest difficulties students face when learning about the mechanism of action of these compounds are related to spatial perception and the configuration of molecules and proteins, ROBERTSON & JORGENSEN (2015). This topic is taught using flat diagrams that seek to represent the interactions between the drug and the receptor binding sites. HALL et al. (2017).

The complexity of the interaction between a drug and its receptor determines its specific mechanism of action. For example, when dopamine receptors are blocked by FNZ, biochemical processes leading to sedation are triggered. Students can thus better visualize this process when they work with physical models. HALL et al. (2017).

Three-dimensional (3D) printing technology can be used to create models for various purposes. The construction and use of synthetic models produced by 3D printing have become increasingly popular. Several studies have pointed to the possibility of using three-dimensional parts as a teaching resource in veterinary medicine. DA SILVA et al. (2023); LIMA et al. (2019); BORGEAT et al. (2022). However, there has been little research on the use of 3D printing in the field of veterinary anesthesiology NEVES et al. (2020).

In this context, the present study evaluated the use of 3D models representing the mechanism of action of FNZ and BUT as tools in the teaching and learning processes of pharmacology and anesthesiology in veterinary medicine. We hypothesized that three-dimensional models would be more efficient at raising students' level of learning compared with flat diagrams. This hypothesis was tested by comparing the acquired level of learning according to students' correct answers before and after the pedagogical intervention.

MATERIALS AND METHODS

Building the models

Pharmacology textbooks were used to select schemes representing the mechanisms of action of FNZ and BUT. Digital models were subsequently created using the *Tinkercad*®. The printing and finishing of the models were conducted at the 3D Educational Technologies Laboratory of the Universidade Federal do Acre, Brazil (Ufac). The FNZ-BUT3D models were made from white acrylonitrile-butadiene-styrene (ABS) filaments to print the models at a 20% fill level. GTMax3D® (GTMax, Americana, Brazil) closed-tray printers were printed using the parts. Post-processing included removal of the support structures, sanding, applying a primer base, painting, and applying varnish.

Evaluation of 3D models

Research participants

This project was submitted to the Ethics Committee for Research with Human Beings of the Ufac and approved by substantiated opinion 69708723.1.0000.5010 (Opinion Number: 6.311.496). All participants signed a Free and Informed Consent Form. Thirty-eight students from the Veterinary Medicine course at UFAC participated in the study. All participants were from the same academic year of the Veterinary Medicine program, and the groups were composed of students with broadly comparable academic backgrounds. The students were divided into two groups of 19 students: a control group (CG) and a 3D group (G3D). The CG students were given lectures comprising dialogues and diagrams of the mechanisms of action printed on paper. G3D received theoretical lessons associated with the use of the FNZ-BUT3D models.

Teaching methodology and data collection

The activity with the students took place over four lessons lasting 50 minutes each, over two different classes of the Veterinary Medicine course at Ufac. After obtaining informed consent forms, the students who agreed to participate in the study completed the pre-test. To assess the students' prior knowledge of the subject, this questionnaire comprised ten multiple-choice questions, five of which were related to the mechanism of action of FNZ and BUT, and five questions about the function of these drugs in the animal's body.

After the pre-test, two lectures were held on the groups of drugs in question, emphasizing their mechanisms of action and effects on animals.

The students in each group were subsequently divided into teams of four to six in the classroom. G3D could handle physical models and assess the main structures and interactions between drugs. In contrast, GC students had access to flat images, with diagrams representing the FNZ and BUT mechanisms. Subsequently, the students in each group answered the post-test, which consisted of the same questions as the pre-test. Finally, G3D answered a satisfaction questionnaire consisting of eight Likert-scale questions and two open-ended discursive questions.

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Statistical analysis

Scores from the pre- and post-test questionnaires for CG and G3D were subjected to the Shapiro–Wilk Normality Test. For data that showed normal distribution, the paired Student's t-test was used for dependent samples (pre-vs. post-tests) and the unpaired Student's t-test for independent groups (mean gain CG vs. G3D). The Wilcoxon test for dependent samples (pre-vs. post-tests) and the Mann–Whitney test for independent samples (gain CG vs. G3D) were used for analyses in which the data were not normally distributed. A significance level of 5% ($P < 0.05$) was adopted. The data were tabulated using Microsoft Office 365 software and processed using JAMOVI software (https://www.jamovi.org/).

RESULTS AND DISCUSSION

Each set of models (Figure 1) comprised a cytoplasmic membrane with three dopamine receptors, as well as structures that mimicked dopamine, FNZ, and BUT. After these parts were created on the platform, the files were downloaded in *stl* extension and converted to the GTMax3D® printer software.

Printing the models

The models printed in ABS following removal of the support structures. The residue of the supports, roughness, and persistent cavities in the parts were corrected using sanding and priming. At the end of all the finishing stages, the pieces had smooth, shiny surfaces (Figure 2).

Evaluation of the mean pre- and post-test scores

The results of the pre- and post-test questionnaires for the two groups are shown in figure 3. Overall, G3D showed a significant difference in the mean scores for all treatments (mechanism of action, function and total). In CG, despite the increase in scores between the pre- and post-tests, there was a significant difference only when the total number of questions was considered.

Figure 4 presents the average increases in students' grades between the pre- and post-tests. This evaluation considered the students' previous knowledge and how much they were able to learn from the methodology developed in each group. The results showed that G3D had a higher mean gain in scores compared to CG; however, a statistically significant difference was observed only in the mechanism of

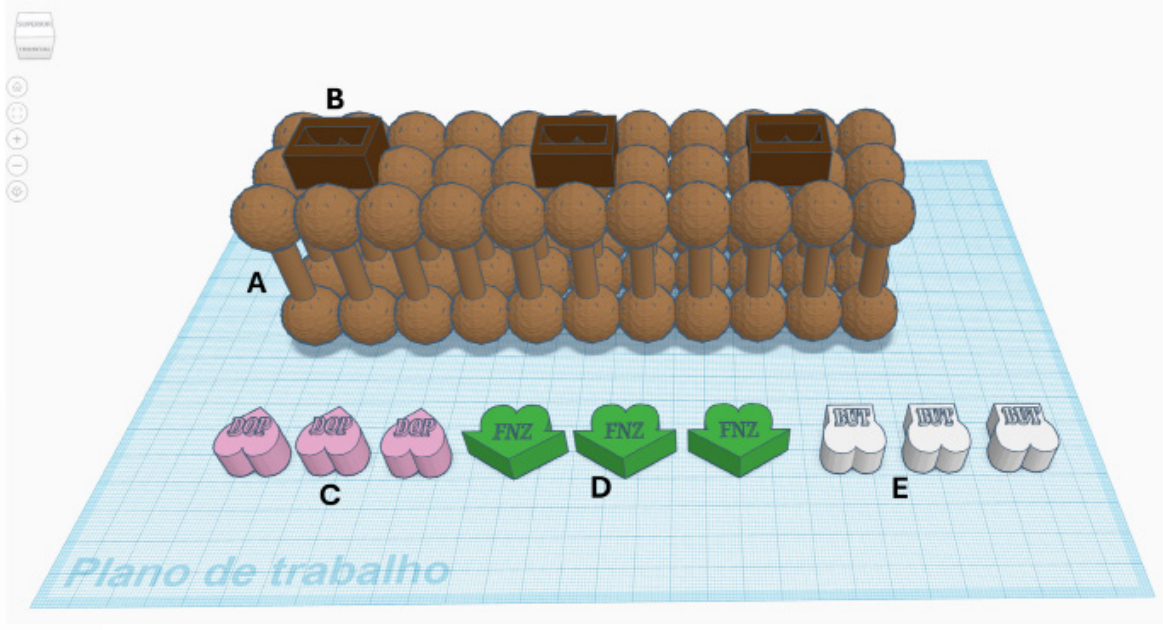

Figure 1 - Three-dimensional digital model developed to illustrate the mechanisms of action of phenothiazines (FNZ) and butyrophenones (BUT) on dopaminergic receptors. (A) Cytoplasmic membrane, represented by a lipid bilayer; (B) dopamine receptors embedded in the membrane, represented by brown structures; (C) dopamine molecules, represented in pink; (D) phenothiazines (FNZ), represented in green; and (E) butyrophenones (BUT), represented in white. The model illustrates the spatial arrangement of these components and serves as a teaching tool to facilitate understanding of the interaction between dopamine, phenothiazines, butyrophenones, and dopaminergic receptors.

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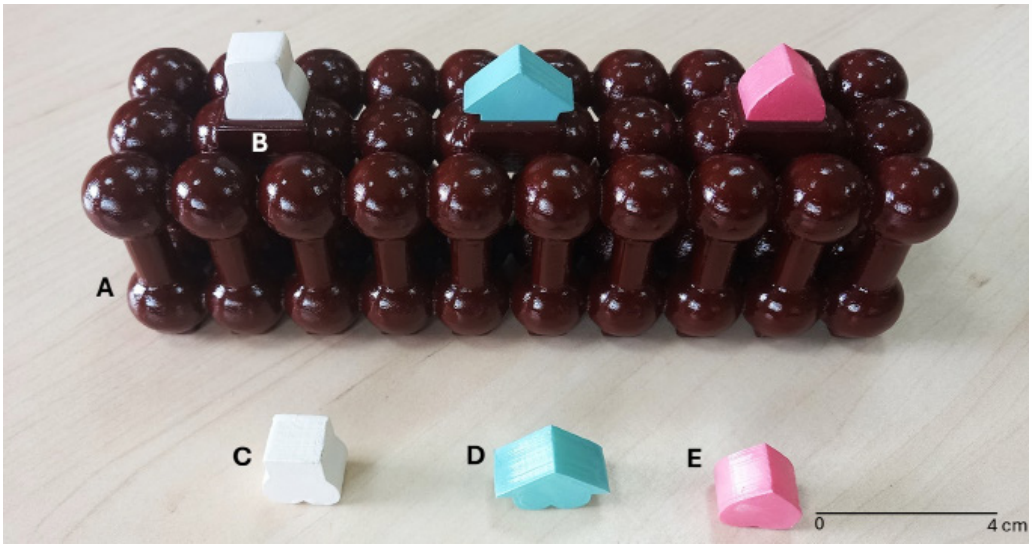

Figure 2 - The finished models after painting and varnishing. (A) Cytoplasmic membrane. (B) Dopamine receptor linked to a BUT. (C) BUT. (D) FNZ. (E) Dopamine. FNZ, phenothiazines; BUT, butyrophenones.

action category. In terms of function and total number of questions, there were no significant differences in the comparisons made.

Evaluation of satisfaction questionnaires

The satisfaction questionnaire is presented in table 1. Figure 5 presents the results of the objective questions in the questionnaire.

In the discursive questions of the satisfaction questionnaire, all answers were positive, indicating that the students enjoyed handling the models, which contributed to learning the subject. Most students pointed out that the use of 3D models improved their level of attention in class. It was also stated that the type of methodology used could guarantee more inclusive teaching, whether for students with disabilities or greater learning difficulties.

DISCUSSION

In terms of the mechanism of action, when comparing the results between the pre- and post-tests, only G3D showed a significant improvement, indicating that FNZ-BUT3D favors student learning. The relative simplicity of the model allowed all students to simulate the stages of the mechanism of action, such as blocking dopamine receptors. It is important to emphasize that the 3D models were designed to represent the initial interaction between the drug and dopamine receptors, serving as a didactic tool to facilitate the visualization of this key step in the mechanism of action. Although, the models do not depict downstream intracellular signaling pathways or systemic physiological effects, they provide a foundational understanding that can support the subsequent integration of more complex pharmacodynamic concepts during theoretical instruction. Therefore, the observed improvements in learning may be associated with enhanced comprehension of the receptor-level interactions, which are essential for understanding the functional consequences of these drugs.

Furthermore, 3D printing technology has the potential to benefit from understanding the mechanisms of action of a chemical substance HALL et al (2017). In this context, the three-dimensional understanding of molecules, through physical or digital models, can also help in the production of new drugs through "reaction design," the process of creating substances for specific applications SMALDONE et al (2023).

The G3D students were the only ones who showed significant improvements in average scores between the pre- and post-tests in terms of the function of FNZ-BUTs in the body. In this context, the three-dimensionality of the models allows students to better understand chemical substances and their pharmacodynamics, as physical 3D models can help to reduce difficulties related to the abstraction of the subject under study, HALL et al (2017); ZHAO et al.

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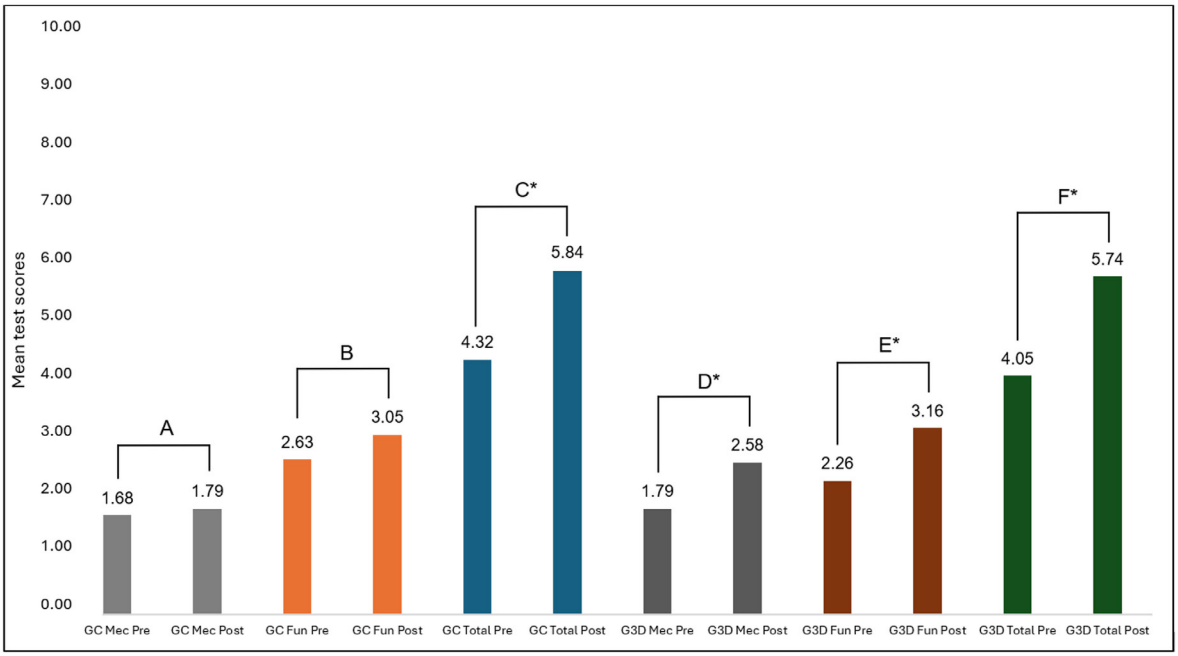

Figure 3 - Mean scores obtained in the pre- and post-tests for the Control Group (CG) and the 3D Group (G3D), considering the categories mechanism of action (Mec), function (Fun), and total score. Data are presented as mean. Standard deviation values (SD): GC Mec Pre = 0.976; GC Mec Post = 0.893; GC Fun Pre = 1.223; GC Fun Post = 0.999; GC Total Pre = 1.688; GC Total Post = 1.268; G3D Mec Pre = 0.893; G3D Mec Post = 1.042; G3D Fun Pre = 1.068; G3D Fun Post = 1.039; G3D Total Pre = 1.431; G3D Total Post = 1.831. Statistical comparisons between pre- and post-tests within groups were performed using paired tests, as described in the methodology. The maximum possible score for each category was 10.0 points.

(2019). It should be noted that abstract elements can be made easier to understand using 3D objects, as they bring theoretical concepts closer to the reality in which the student is inserted CAPELOTO et al (2023).

When evaluating the total average scores (mechanism + function), both groups showed significant improvements, indicating that the different methodologies were effective at promoting pharmacological learning. The similarity between the two methodologies is the effective participation of teachers in class, which shows that their mediation in the learning process is of fundamental importance. Furthermore, our findings corroborated a study that highlighted that teachers' mastery of pedagogical content, self-efficacy, and enthusiasm are essential for improving student engagement and performance, FAUTH et al (2019), as well as for integrating technologies such as 3D printing into their teaching practice.

The average gain in the G3D students' grades reinforces the hypothesis that FNZ-BUT3D models are efficient as a complementary resource to teachers' work in teaching mechanisms of action. In this sense, educational models of molecules, represented in 3D physical pieces can facilitate the understanding of reaction pathways ROBERTSON & JORGENSEN (2015); GORDEEV & ANANIKOV (2020).

Using only one teaching methodology may not be sufficient to meet the specific needs of each student, let alone in a heterogeneous classroom. Indeed, some students learn more from the teacher's explanations or auditory resources, while others are better served by visual methodologies, and others are more kinesthetic, meaning that manipulation and touch become more important, LIMA et al (2019). However, this is not an isolated didactic resource that promotes universal learning in classrooms. Indeed, it is argued that a variety of methodologies, always mediated by the teacher, are more effective at promoting student learning BORGEAT et al (2022); MUNNA & KALAM (2021).

In the satisfaction questionnaire, some students highlighted the quality of the models and stated that they were easy to fit. This positive experience is understandable when considering the importance of the sense of touch in learning. Students' styles of perception, whether auditory,

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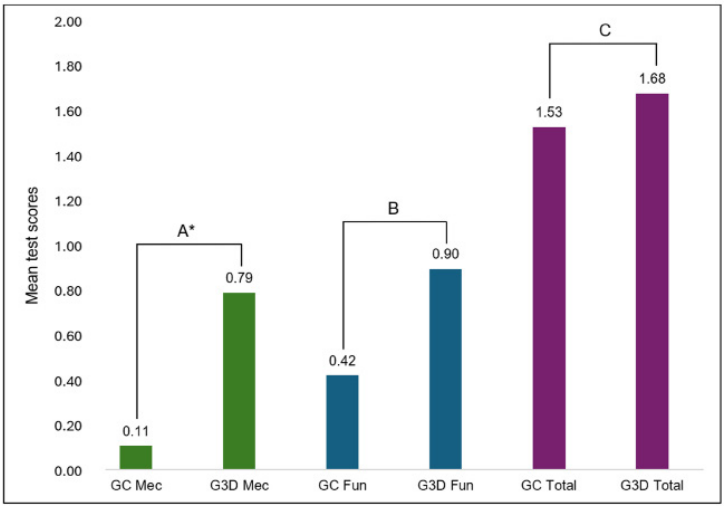

Figure 4 - Mean gain in scores between pre- and post-tests for the Control Group (CG) and the 3D Group (G3D), considering mechanism of action (Mec), function (Fun), and total score. Data are presented as mean. Standard deviation values (SD): GC Mec = 0.968; G3D Mec = 1.055; GC Fun = 1.270; G3D Fun = 0.788; GC Total = 1.094; G3D Total = 1.379. Statistical comparisons between groups were performed using appropriate tests as described in the methodology. A statistically significant difference was observed only for the mechanism of action category (P = 0.043).

visual, or kinesthetic, are related to the way they learn GOULART et al (2021). Although, everyone possesses these three perceptions, only one prevails. Therefore, it is essential that different teaching strategies meet students' learning characteristics. One potential limitation of this study relates to the scope of the content addressed and the number of questions used in the assessments. Although, the findings

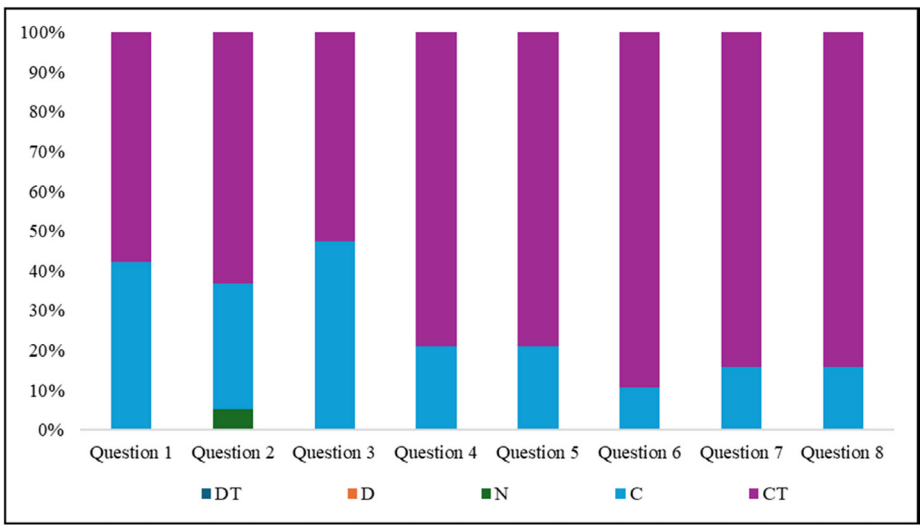

Figure 5 - Evaluation of the answers to the satisfaction questionnaire answered by G3D. The responses were as follows: Totally disagree (DT), Disagree (D), Neutral or Indifferent (N), Agree (C) and Totally Agree (CT), according to the Likert scale.

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Table 1 - Questions asked in the satisfaction questionnaire.

1	Did the use of 3D models make it easier to understand the mechanisms of action?
2	Did the use of 3D models make it easier to understand the effects of drugs on animal patients?
3	Would you be interested in using similar additional templates in the future?
4	Was the 3D model easy to handle and understand?
5	Did the use of 3D models make the lesson more dynamic and interactive?
6	Did the use of 3D models make the lesson more attractive and less abstract?
7	Is the use of 3D models in class an active learning methodology?
8	Would you recommend using such models to future veterinary students?
9	What suggestions would you make to improve the models and methodology used in these classes?
10	What did you like most and least about these lessons? Is there anything else you would like to comment on?

indicated improvements in student performance, future studies including a broader range of topics and more comprehensive assessment tools may help to further refine the interpretation of the educational impact observed.

Overall, the results of this study showed that the 3D models contributed to learning the mechanism of action and functions of FNZ and BUT. These findings converge with the principles of the dual-coding theory (DCT), which addresses the importance of verbal and visual relationships during learning. In the context of DCT, it is believed that when students take part in an oral lesson, at the same time as their auditory sense is required, visual representations of the information received are created FREDERICO & GIANOTTO (2018).

The shapes and colors of the parts that comprised the model (cytoplasmic membrane, dopamine receptor, dopamine, FNZ, and BUT) were also remembered positively by the students in the satisfaction questionnaire. In fact, it has already been shown that three-dimensional models with a good appearance and representativeness are effective at promoting student learning HALL et al (2017); BORGEAT et al (2022).

CONCLUSION

The FNZ-BUT3D models were effective at raising the students' level of learning about the subject, particularly in understanding the mechanisms of action of these drugs. It is believed that the adoption of methodologies that consider visual, auditory, and kinesthetic aspects met the different perception characteristics of the students, with the irreplaceable presence of the teacher in mediating the teaching and learning processes.

DATA AVAILABILITY STATEMENT

The raw data supporting the findings of this study, including individual pre- and post-test scores and responses to the student satisfaction questionnaire, are available from the corresponding author upon reasonable request. To protect participants' confidentiality, data will be shared in de-identified form and in accordance with applicable ethical requirements.

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DECLARATION OF CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest related to this work.

AUTHORS' CONTRIBUTIONS

ALS contributed to conceptualization and methodology, developed the three-dimensional models, collected the data, performed the statistical analysis, and wrote the original manuscript. RGS contributed to model development, data collection, statistical analysis, manuscript writing, and writing – review and editing. MECNO contributed to manuscript submission and writing – review and editing. RCSS contributed to manuscript submission and writing – review and editing. YKC supervised the project, provided guidance throughout all stages, contributed to writing – review and editing, and approved the final version of the manuscript.

BIOETHICS AND BIOSECURITY COMMITTEE APPROVAL

Federal University of Acre - UFAC Substantiated Opinion from the CEP RESEARCH PROJECT DATA; Research

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Title: THREE-DIMENSIONAL MODELS FOR TEACHING THE MECHANISMS OF ACTION OF PRE-ANESTHETIC DRUGS (MPAs) IN VETERINARY MEDICINE; Researcher: ALCIDES LOUREIRO SANTOS; Thematic Area: Version: 2 CAAE: 69708723.1.0000.5010; Proponent Institution: Graduate Program in Animal Health and Sustainable Production Main Sponsor: Universidade Federal do Acre - UFAC OPINION DATA Opinion Number: 6.311.496

DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE

During the preparation of this manuscript, ChatGPT (OpenAI) was used as an editorial support tool to assist with English-language refinement, improvements in clarity and consistency. The authors reviewed and verified the AI-assisted suggestions and retained full responsibility for their incorporation into the manuscript. The use described here did not involve generating or analyzing research data, conducting the experiments, or formulating scientific findings or conclusions. The authors take full responsibility for the accuracy, originality, and scientific integrity of the final manuscript.

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