The American Journal of Medical Sciences and Pharmaceutical Research ISSN 2689-1026 Volume 08 - 2026

Studies On The Cumulative Effect And Toxicity Of The Dental Gel "Benzpaya-S"

[1] Rakhmanova Zarina Abdukarimovna
[1] Tillayeva Umida Makhmudzhanovna
[1] Tillayeva Gulnora Urunbayevna

[1] Tashkent Famaceutical Institute, Tashkent, Uzbekistan

Received: 31 Dec 2025 | Received Revised Version: 16 Jan 2026 | Accepted: 03 Feb 2026 | Published: 21 Feb 2026

Volume 08 Issue 02 2026 | Crossref DOI: 10.37547/tajmspr/Volume08Issue02-15

Abstract

Studies were conducted to study the toxicological effects: safety and cumulative effect of a new combined dosage form in the form of gels based on benzketosone and papaya extract. Experiments were performed on oral wounds and cutaneous wounds in an experiment on rats. A comparative analysis of the wound-healing effect of the new composition of gels "Benzpaya" was carried out with the comparison preparations gels Asepta and Salcoseril, the advantage of the former was revealed. The developed gel can become an alternative tool in the treatment and prevention of dental diseases with minimal risk of side effects. The new composition of gels "Benzpaya" in a dose of 150 mg / kg has a wound-healing effect, which reduces the time of cleansing and wound healing by 4-8 days. A comparative analysis with the comparison drugsgeli Asepta and Salcoseril revealed the advantage of the former.

The results of studying the acute toxicity of the new composition of gels "Benzpaya-S" showed that they belong to the VI class of relatively harmless substances. LD5050in mice when administered into the oral cavity was more ≥than ≥5000 mg/kg. There is also a lack of not only cumulative action, but also habituation.

Keywords: Dental diseases, nonsteroidal anti-inflammatory drugs, phenylglyaxic acid, benzketosone, papaya, gengivitis, stomatitis.

Cite This Article: Rakhmanova Zarina Abdukarimovna, Tillayeva Umida Makhmudzhanovna, & Tillayeva Gulnora Urunbayevna. (2026). Studies On The Cumulative Effect And Toxicity Of The Dental Gel "Benzpaya-S". The American Journal of Medical Sciences and Pharmaceutical Research, 8(2), 100–107. https://doi.org/10.37547/tajmspr/Volume08Issue02-15

1. Introduction

Dental diseases, including inflammatory processes in the oral cavity, such as stomatitis and gengivitis, remain an urgent problem among the population of Uzbekistan. According to WHO data, about 60% of the country's adult population suffers from oral diseases (1,2,3). One of the promising areas is the use of developments of domestic medicines and biologically active substances based on natural and synthetic components.

Phenylglyoxylic acid derivative domestic non-steroidal anti-inflammatory drug Benzketozone, was approved for use by the Main Directorate for Quality Control of

Medicines and Medical Equipment of the Ministry of Health of the Republic of Uzbekistan tablets (0.1 g of active substance) VFS 42 Uz-0663-2003 and ointments (0.5% and 3%) of FSP 42 Uz-0186-2007. 3% Benzketozone ointment in accordance with the order of the Ministry of Health of the Republic of Uzbekistan is allowed for the treatment of inflammatory viral diseases (konyuktevitis, colpitis, as part of complex therapy (FSP 42 Uz - 0186-2007) [4,5]. The efficacy of Benzketosone in clinical trials was evaluated in comparison with the steroid anti-inflammatory drug 0.5% hydrocortisone eye ointment. Experiments on various animals have shown that benzketosone has a high anti-inflammatory activity and low toxicity. It should also be noted the importance of using enzyme preparations in combination with nonsteroidal anti-inflammatory drugs and their strengthening effect [6].

Purpose of the study. Studyof toxicological effects: acute toxicity and cumulative action (on the model of stomatitis) and wound-healing activity of a new combined dosage form in the form of a gel based on benzketozone and papaya extract "Benzpaya-S".

2. Methods

Gelfor dentistry - "Benzpaya-S", aluminum tubes of 20 g, with

With the content of benzketosone 0.1 g, papaya fruit extract 10 g ser. 10 09 23, experimental laboratory samples were developed and obtained at the Department of Organization of Pharmaceutical Production and Quality Management of the Tashkent Pharmaceutical Institute.

Combined gel "Asepta" with propolis content (comparison drug), ser. 12.01.21. produced by the pharmaceutical company JSC VERTEX, Russia. And Salkoseril gel is a medicinal product produced by LEGACY PHARMACEUTICALS SWIZERLAND, GmbH (Switzerland). The research was conducted at the Belgorod Institute of Pharmacy, Chemistry and Biology, in the Laboratory of Pharmacology with the consultation of Doctor of Biology Prisny A. A.

The general effect and acute toxicity of the new composition of the combined gels "Benzpaya-S" were performed according to the Sanotsky method. To determine the parameters of acute toxicity, the Litchfield and Wilcoxon method was used [7]. The study of acute toxicity of the drug was carried out on white outbred mice, males weighing 20±2.0 g, 5 animals in each group, a total of 25 mice were used. Gel for dentistry was applied in the oral cavity, in doses of 2000, 2500, 3000, 4000 and 5000 mg/kg. The last two doses are divided after 1 hour.

All pharmacological studies were performed on healthy sexually mature animals (mice) that were quarantined for at least 10-14 days. At the same time, the general condition, behavior and death of animals were taken into account. The animals were monitored hourly during the first day of the experiment in the laboratory, while survival during the experiment, general condition, possible convulsions and death were used as indicators of the functional state of the animals. Then, every day, for 2 weeks in a vivarium, animals of all groups were monitored for general condition and activity, behavioral characteristics, frequency and depth of respiratory movements, condition of hair and skin, tail position, changes in body weight, etc. indicators.

All experimentalanimals were kept under normal vivarium conditions at a temperature of 23-260C, on a general diet with free access to water and food. At the end of the experiment, the average lethal dose (LD50) was calculated50and the toxicity class was determined (8,9).

The cumulative properties of the "Benzpaya-S"gelwere studied by the subchronic toxicity method,according to the method of Lima et al., which makes it possible to assess not only accumulation, but also addiction. Experiments were performed on 10 rats of both sexes weighing 200±15.0 g. Treatment was performed 2 hours after the experimental model of the disease was induced, by injecting the gel under study into the oral cavity of guinea pigs.

After determining the cumulative property гелявof the"Benzpaya-S"gel, the animals were decapitated for pathomorphological examination of internal organs, with the calculation of an integral indicator-the mass coefficient (MC). Analysis of this indicator makes it possible to detect target organs with a pathologically relatedм effect. Organs extracted at autopsy are weighed wet to avoid drying out, and paired organs are weighed together. MC is calculated using the formula: MC = Organ weight (g)/body weight (g)×100%.

Statistical processing of the obtained data was performed using Microsoft Office Excel and Staticrica 6.0 computer programs.

In the second series of experiments, the anti-inflammatory activity of the gel"Benzpaya-S" was studied on the model of experimental stomatitis, corresponding to stomatitis, andreparative activity on the model of alternative inflammation of skin wounds.

Model of experimental stomatitis

The anti-inflammatory study was conducted on 25 guinea pigs weighing 300-350 g, 5 males in each experimental group. A model of inflammation of experimental stomatitis in animals was induced введением by injecting 0.15 ml of 25% formalin into the oral cavity of pigs with formalin.

Treatment was carried out 2 hours after the experimental model of the disease was induced, by injecting guinea pigs with "Benzpaya-S" gel ata dose of 150 mg / kg. The dose was calculated according to the guidelines for the development of drugs and BAS [7]: 1600 mg per person:70kg=(mg / kg) x 39(human): 6 (guinea pig) mg/kg.

The comparison drug was a combined gel "Asepta" with propolis content, and "Salcoseril" drug, deproteized dialezate from the blood of healthy dairy calves (in terms of dry matter) 4.15 mg, 20 g each-an anti-inflammatory and regenerating agent.

Систематически в условиях экспериментального исследования Changes in the skin of the oral mucosa were systematically observed in the experimental study on days 3, 7, 14 and 21 after oral administration of formalin. The severity of the developing disease was judged by the general condition (general appearance, condition of the coat, discharge from the oral cavity, weight dynamics) and behavior (motor activity aggressiveness, appetite). At the same time, the temperature of guinea pigs was recorded using an electronic thermometer. In addition, peripheral blood was examined: the content of hemoglobin, g / l, the number of red blood cells,10-12/l and leukocytes109/l on a hematological analyzer Diatron Ltd, 2002 (Hungary).

Model of alternative inflammation (model of skin wounds).

Модель кожнThe skin ras model was performed on 25cattle (males) weighing 200-215 g, 5 heads in each experimental group. In rats anesthetized with sodium ethamine (dose 50 mg/kg, iv), under aseptic conditions, a standard diameter and depth skin wound of 1.0 x 1.0 cm and 0.5 mm deep was applied to the pre-depilated surface of the back skin.0,5 ммThe wounds were left open [2,3].

Treatment was started immediately after reproduction of the experimentally induced pathology. The test gels were administered until complete recovery (21 days). Nothing was administered to the control group of animals. The wounds remained open. Follow-up periods are 1, 3, 7, 14, and 21 days after the start of the experiment. The rate of wound healing was estimated by:

1. by the presence of wound exudate and its cellular composition;

2. according to the condition of the adjacent tissues;

3. by changing its area, mm2.

3. Results

Studies of the general effect and acute toxicity of the gel "Benzpaya-S" were conducted on healthy laboratory animals, white outbred male mice weighing 18-22 g. Before starting the experiment, the animals were kept in quarantine for 10 days. As mentioned above,the drug was applied in doses of 2000, 2500, 3000, 4000 and 5000 mg/kg.

Monitoring of the animals ' condition after applying the drug was carried out for 2 days in the laboratory and 14 days in the vivarium.

During the period of observation of animals, the main attention was paid to the general condition, relaxation of the tone of skeletal muscles and legs, the state of the pupil of the eyes, and the reaction to external stimuli.

Experimental studies have shown that when a new composition of gels "Benzpaya-S" is introduced into the oral cavity at a dose of 2000-5000 mg/kg in animals, it does not cause any negative reactions, as well as pathological changes.

Analysis of the general condition of the animals showed that no significant differences in weight were observed in the animals that received the new composition of "Benzpaya-S" gels. All animals showed a satisfactory appetite. No animal deaths were observed during the observation period (Table 1).

Table 1

Results of indicators of "acute" toxicity after oral administration of the new composition geli "Benzpaya-S" to mice

Drug, type of animal, route of administration	sex	Dose mg / kg	Number of animals in the group / number of deaths	LD_{16} -m+m mg/kg	LD_{50} -m+m mg/kg	LD_{84} -m+m mg / kg	Total effect
of mice oral	administration males	2000	6/0	-	≥5000		The drug does not cause any negative reactions or pathological changes in animals.
		2500	6/0				
		3000	6/0				
		4000	6/0				
		5000	6/0				

Consequently, the results of studying the acute toxicity of the new composition of gels "Benzpaya-S" showed that they belong to the VI class of relatively harmless substances. LD5050in mice when administered into the oral cavity was morethan ≥5000 mg/kg.

In the second series of experiments, the anti-inflammatory activity of the studied drugs and their effect on the treatment of experimental stomatitis were studied.

Against the background of a model of experimental stomatitis induced by 25% formalin solution, treatment was carried out in five groups: in the first group of animals, placebo gel was administered, this group was a control group,inthe second group of animals, Benzpaya-S gel was administered, at a dose of 150 mg / kg, in the third and fourth groups, experimental stomatitis was treated with comparison drugs combined gel "Asepta" with propolis content, and dental gel "Salkoseril".

At the time of formalin injection into the oral cavity, all animals showed arousal, which was expressed in increased motor activity and increased breathing. After 3-4 hours, the animals showed sharp aggressiveness, which persisted to the control group until the end of the experiment.

In theexperimental animals of the control group, both the local inflammatory reaction and its general manifestations increased one day after the pathology was reproduced. The most striking symptoms during this period include sharp redness of the mouth, the mucous membrane of which is hyperemic and edematous. In the following days, local inflammatory reactions appeared, blood on the mucosa, mucosal discharge and swelling were observed. On day 3-7 of the study, blood and purulent formations of aphids were observed. At the same time, guinea pigs become pasty. On days 14-21 of the experiment, the general condition of the animals was restored to the initial state. The duration of the course of the process of experimentalstomatitiswas observed up to 14-21 days in the experiment.

The treated animals were better able to tolerate the damaging effect of formalin on the oral mucosa. The first clinical signs of the disease, as in the control group, appeared one day after the pathology was reproduced.

In the experimental group, when using the testgel andов the comparison drug, these changes were manifested in a mild form. Symptoms of local inflammation on day 3 of the experiment were more pronounced, but blood with mucus, swelling and discharge from the mouth, compared with animals in the control group, on average

decreased by 1.5-2 times, there was no bleeding and manifested in 50% of animals. However, after 5-7 days of treatment, the general condition of the treated animals improved. The guinea pigs showed their usual activity.

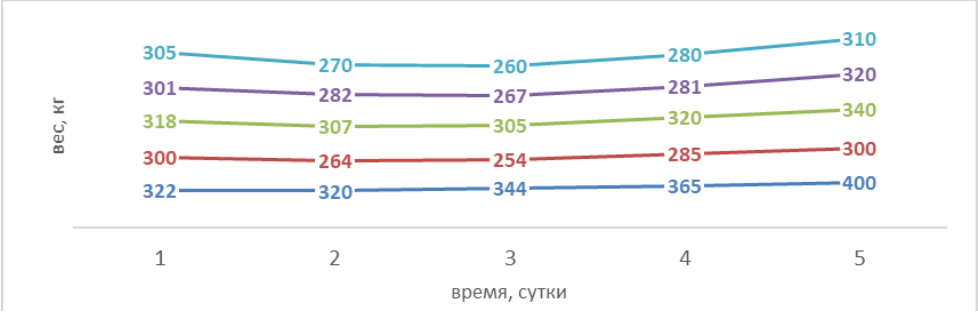
On the 7th day of the study, experimental animals showed a decrease in body weight of animals, both in the control group by 26%, andin the experimental groupswith the introduction of the dental gel composition by 10% and the comparison drug in Asept and Solcoseryl by 22.3% and 24.4%, respectively. On day 21, we observed in the control group and the group treated with the comparison drug the animals 'body weight returned to the initial values, and in the group treated with the composition of gels" Benzpaya-S " - on day 14. It should be noted that 2 out of 5 control animals died on day 6-7, which was accompanied by a sharp drop in body weight. In the experimental groups, there were no deaths of animals (Table 2, Fig.1).

Table2

Effect of the Benzpaya-S gel composition on the weight of guinea pigs with experimental stomatitis (M±m; n=5)

Experimental condition, dose, mg / kg	Animal weight, kg / study days				
	Outcome	3	7	14	21
Intact animals	322±16,3	330±12,4	344±12,5	365±14,5	400±15,0
Control (untreated animals)	300±16,3	264±12,4	254±12,5	285±14,5	300±15,0
New song **gels "Benzpaya-S"**	318±13,5	307±13,0	310±13,8	320±13,9	340±14,8
Asept Gel	301±13,5	282±13,0	267±3,8	281±13,9	320±14,8
Salcoseryl Gel	305±13,0, 0	270±11,0, 0	260±3,11	280±13,44	310±13.0, 0

* P< 0.05 in relation to the control group.



- Intact animals
- Control
- New composition of geli "Benzpaya-S"
- Asept Gel
- Salcoseryl Gel

1 Influence of the new composition of gels "Benzpaya-S" on the weight of guinea pigs with experimentalstomatitis.

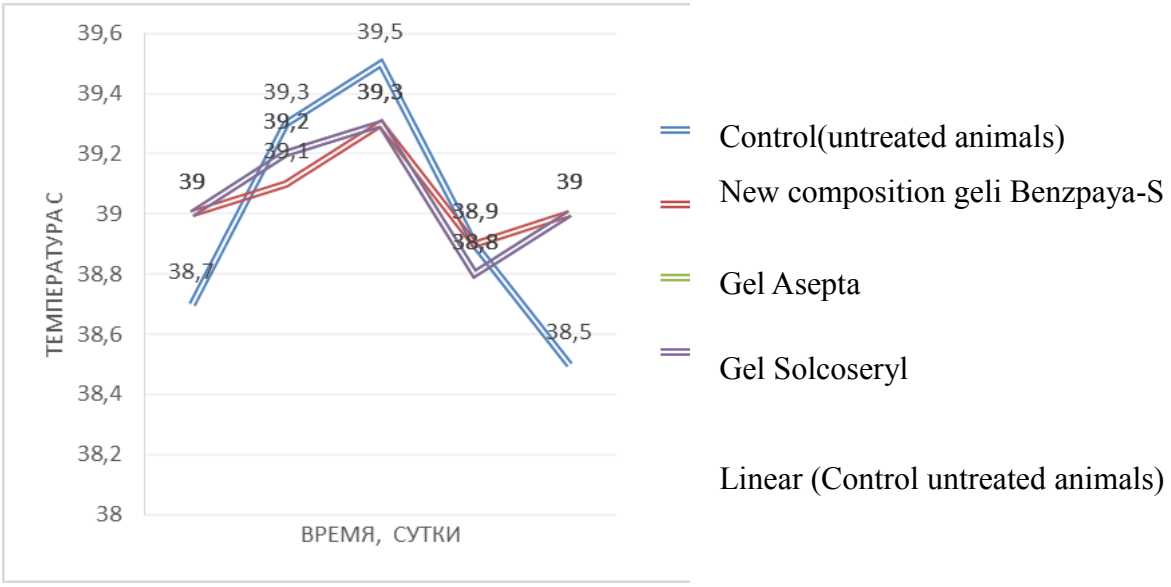
Manifestations of the severity of local inflammation and general intoxication were an increase in rectal temperature by 0.6-0.80S for 3-7 days. In the groups of animals treated with the new composition of gels "Benzpaya-S" and the comparison drug gel Asepta and gel Solcoseryl, the temperature reaction was smoothed and short-lived. Its maximumpeak did not exceed 0.3-0S (Table 3).

Table 3.

Effect of the new composition of gels "Benzpaya-S" on the rectal temperature of guinea pigs (M±m; n=5)

Experimental condition, dose, mg / kg	Rectal temperature, ^{0}C / study days				
	Outcome	3	7	14	21
Control (untreated animals)	38,7±3,2	39,3±3,2*	39,5±3,2*	38,9±3,2*	38,5±3,2*
New composition gels "Benzpaya-S"	39,0±3,2	39,1±3,2	39.3±3.2	38.9±3.2	39.0±3.2
Asept Gel	39,0±3,2	39,2±3,2	39,3±3,2	38,8±3,2	39,0±3,2

*P≤ 0.05 relative to the outcome



2. The effect of the new composition of "Benzpaya-S" gels on the rectal temperature of guinea pigs with experimentalstomatitis.

Significant changes were observed in the peripheral blood parameters. In the first three days after the pathology was reproduced, the number of white blood cells increased by 30%, the maximum leukocytosis was observed on days 7-14 (65-100 %).

As the inflammatory process increased, all animals showed signs of impaired erythropoiesis. In the control group, after 7-14 days of the first experiment, the hemoglobin level decreased by 21-10 %, the concentration of red blood cells by 30-31%, and returned to normal on day 21.

Changes in the peripheral blood of treated animals had

some features, leukocytosis, as a rule, was less pronounced.

The level of hemoglobin decreased to a lesser extent than in the control group of animals, and by day 7 it reached the initial values. The concentration of red blood cells did not decrease significantly (Table 4).

See Table 4.

Effect of the new composition of gels "Benzpaya-S" on the morphological composition of peripheral blood of guinea pigs with experimental stomatitis (M±m; n=5)

Indicators of	study Days				
	INTAKT	Control	Composica gels "of Bespa With"	Asepta Gel	Gel Solkoseril
after 3 days,					
Hemoglobin, g/l	10,5±0,4	8,8±0,3	10,6±0,2	9,3±0,2	8,9±0,5
Erythrocytes, 10 ^{12}/l	5,9±0,5	4,6±0,2	5,8±0,3	4,3±0,3	4,0±0,4
Leukocytes,10^{9}/l	9,2±1,0	13,5±1,1	10,0±1,2	9,8±1,1	11,2±1,5
7 days					
Hemoglobin, g/l	11,0±0,4	8,2±0,3	11,3±0,2	9,3±0,2	9,0±0,1
Erythrocytes, 10 ^{12}/l	6,0±0,5	4,0±0,2	7,0±0,3	4,8±0,3	4,8±0,3
Leukocytes,10^{9}/l	9,0±1,0	19,2±1,1	9,25±1,2	8,2±1,1	8,0±1,1
after 14 days,					
Hemoglobin, g/l	11,0±0,4	8,8±0,3	12,0±0,2	10,1±0,2	9,5±0,2
Erythrocytes, 10 ^{12}/l	6,0±0,5	4,3±0,2	7,4±0,3	5,2±0,3	5,0±0,3
Leukocytes,10^{9}/l	10,0±1,0	15,25±1,1	11,0±1,2	10,0±1,1	9,0±0,8
21 days					
Hemoglobin, g/l	10,5±0,4	9,6±0,3	11,0±0,2	10,3±0,2	10,0±0,1
Erythrocytes, 10 ^{12}/l	5,8±0,5	5,0±0,2	6,8±0,3	5,7±0,3	5,3±0,2
Leukocytes,10^{9}/l	10,5±1,0	12,25±1,1	9,0±1,2	10,8±1,1	10,8±1,1

*P<0.05 relative to the control

Based on the results of the pharmacological study, it can be concluded that the preparation of the new gel "Benzpaya-S" has an anti-inflammatory and reparative effect characteristic of its components, having a favorable effect on the course of experimental stomatitis.

4. Conclusions

Based on the results of the pharmacological study, it can be concluded that the preparation of the new composition of gels "Benzpaya-S" has an anti-inflammatory and reparative effect characteristic of its components, exerting a favorable effect on the course of experimental stomatitis.

The new composition of gels "Benzpaya"in a dose of 150 mg / kg has a wound-healing effect, which reduces the time of cleansing and wound healing by 4-8 days. A

comparative analysis with the comparison drugsgeli Asepta and Salcoseril revealed the advantage of the former.

The results of studying the acute toxicity of the new composition of gels "Benzpaya-S" showed that they belong to the VI class of relatively harmless substances. LD5050in mice when administered into the oral cavity was more than ≥5000 mg/kg.The cumulative property of the gel was studied by the subchronic toxicity method, according to the Lima method. The results showed the absence of not only accumulation, but also habituation.

References

1. Dental diseases (Stomatitis, Gingivitis) https:// www/sm-stomatology.ru/
2. Study of dental gel with dry extract and camel thorn.Akhmetkand.A., Turgunbayeva A. A., Burasheva G. Sh., Ustenova G. O. Collection of Mat. XIII-th Intern. scientific and practical conferences "Priorities of Pharmacy and Dentistry: from theory to practice" dedicated. to the 135th anniversary of S. D. Asfendiyarov, NAO KazNMU, Alma-Ata, 2024-pp. 1-21.
3. Sapovskaya A.V., Sampiev A.M., Nikiforova E. B. Actual issues, nomenclatures, properties and technologies of dental gels //Modern problems of science and education.-2015. - No. 1. - p. 128
4. Zakirov U. B., Maksudov A. A., Azizov U. M. Study of the effectiveness of benzketozone in the treatment of eye burns. Pharmaceutical magazine. Tashkent, 2004; 1: 90-92.
5. 5.Pharmacopoeia. Petrol filling station. 42 Уз-0850-2010,42-Уз-0850-2020
6. Tillaeva U.M., Nazarkulov M.S., Rahmanov Z.A., Tillaeva G,U., Gaibnazarova D.T. Analysis of drugs containing enzymes in the pharmaceutical market of the republic of Uzbekistan. World journal of Pharmaceutical and life sciences. 2020;6(1):01-04.
7. Methods of testing the effects of chemical products on the human body. Acute oral toxicity-method for determining the class of acute toxicity. (OECD, Test No. 423: 2001,IDT) Minsk 2013.
8. Methodological recommendations for the preclinical study of dermatotropic medicinal products /Guidelines for conducting preclinical studies of medicinal products. Part One, Moscow, 2012, pp. 738-746. Mironova A. N.
9. Glyantsev S. P., Annaeva A. G., Savina T. V. Morphological substantiation of the choice of composition and structure of biologically active composition based on sodium analginate for the treatment of wounds. biol. and medicine. 1999. No. 1. pp. 65-67.
10. C.Y. Hsu, M.J. Saadh, A.F. Mutee, H. Mumtaz, G.U. Tillaeva, M. Mirzaei, M. Da'i, F. Mascarenhas-Melo, M.M. Salem-Bekhit. Assessing the metronidazole adsorption by an iron-enhanced nanocone along with DFT calculations regarding the conjugated system formations for developing the drug delivery platforms,Inorganic Chemistry Communications,Volume 165,2024,112496,ISSN 1387-7003,https://doi.org/10.1016/j.inoche.2024.112496.
11. M.C. Bautista, D. Cort´es-Arriagada, E. Shakerzadeh, E.C. Anota, Acetylsalicylic acid interaction with Boron nitride nanostructures–a density functional analysis, J. Mol. Liq. 355 (2022) 118980.