https://dergipark.org.tr/tr/pub/ataunivbd
2019; 14(3): 335-342

Review/Derleme
DOI: 10.17094/ataunivbd.567915

Atatürk Üniversitesi Veteriner Bilimleri Dergisi
Atatürk University Journal of Veterinary Sciences

Application of Xanten and Its Derivatives in Human and Veterinary Medicine

Alisa SMAJOVIĆ[1a], Muhamed KATICA[2b], Davorka ZAVRŠNIK[3c], Elma VELJOVIĆ[3d]✉, Kenan ČAKLOVICA[4e]

1. University of Sarajevo, Faculty of pharmacy, Department of pharmaceutical informatics and pharmacoeconomics, Sarajevo, BOSNIA and HERZEGOVINA.
2. University of Sarajevo, Veterinary Faculty, Department of Pathological Physiology, Sarajevo, BOSNIA and HERZEGOVINA.
3. University of Sarajevo, Faculty of pharmacy, Department of Pharmaceutical Chemistry, Sarajevo, BOSNIA and HERZEGOVINA.
4. University of Sarajevo, Veterinary Faculty, Department of meat hygiene and meat products, Sarajevo, BOSNIA and HERZEGOVINA.
ORCID: 0000-0002-2497-6744[a], 0000-0002-8184-0065[b], 0000-0001-6486-6813[c], 0000-0003-1129-1491[d], 0000-0001-7506-5843[e]

Geliş Tarihi/Received	Kabul Tarihi/Accepted	Yayın Tarihi/Published
20.05.2019	23.09.2019	25.12.2019

Bu makaleye atıfta bulunmak için/To cite this article:
Smajović A, Katica M, Završnik D, Veljović E, Čaklovica K: Application of Xanten and Its Derivatives in Human and Veterinary Medicine. Atatürk University J. Vet. Sci.,14(3): 335-342, 2019. DOI: 10.17094/ataunivbd.567915.

Abstract: Xanthene derivatives represent cyclic, organic compounds that can be natural, semi-synthetic and synthetic origin. These compounds become very interesting because of various pharmacological activities such as antibacterial, antiviral and anti-inflammatory properties. Furthermore, they have been utilized as antagonists for drug-resistant leukemia lines and in photodynamic therapy. They are also applied as dyes in laser technology and pH sensitive fluorescent materials for visualization of biomolecules. Because of new diseases in veterinary medicine, application of these compounds can be very useful and literature describes activity of similar compunds in veterinary research field. In this review the most important activity of xanthen derivatives such as antibacterial, antifungal, antihelmintic, antiprotozoal, anticancerogenic and antidiabetic activity and mechanism of their action are presented.

Keywords: Xanthene derivatives, Pharmacology activities, Veterinary medicine.

Xanten ve Türevlerinin İnsan ve Veteriner Hekimlikte Kullanımı

Öz: Ksanten türevleri, doğal, yarı sentetik ve sentetik kökenli olabilen siklik, organik bileşikleri temsil eder. Bu bileşikler, antibakteriyel, antiviral ve antienflamatuar özellikler gibi çeşitli farmakolojik aktiviteler nedeniyle dikkat çekmektedirler. Ayrıca, ilaca dirençli lösemi hatları için ve fotodinamik tedavide antagonistler olarak kullanılmaktadırlar. Ayrıca lazer teknolojisinde boyalar ve biyomoleküllerin görselleştirilmesi için pH'a duyarlı floresan malzemeler olarak uygulanırlar. Veteriner hekimlik alanında yeni hastalıklar nedeniyle, bu bileşiklerin uygulanması çok faydalı olabilir ve literatürde Veteriner araştırma alanındaki benzer bileşiklerin aktivitesi açıklanmaktadır. Bu derlemede ksanten türevlerinin antibakteriyel, antifungal, antihelmintik, antiprotozoal, antikanserojenik ve antidiyabetik aktivite gibi en önemli aktiviteleri ve etki mekanizmaları sunulmuştur.

Anahtar Kelimeler: Ksanten türevleri, Farmakolojik aktiviteler, Veterinerlik.

✉ Elma Veljović
University of Sarajevo, Faculty of pharmacy, Department of Pharmaceutical Chemistry, Sarajevo, BOSNIA and HERZEGOVINA.
e-posta: elma.veljovic@ffsa.unsa.ba

INTRODUCTION

The spread of zoonoses from animals to humans has been specifically described from 20th to the 21st century. It is evident that these zoonoses often cause high mortality or create enormous financial losses in livestock production. The worrying phenomenon is the so-called. "technopathy" occurring in intensive livestock production, where a large number of animals are intensively raised in a relatively small area with the aim of obtaining extra profits. In such an unnatural environment for animals, new diseases of unclear etiology are emerging, and definitely new drugs are needed to be effective in preserving the health of people and animals.

Resistance to already known antibiotics is a burning problem. Drugs that have antibacterial activity increasingly show weaknesses in the fight against various strains of bacteria. Bacterial cells most often produce resistance not only through one, but also through multiple mechanisms, so there is a known high resistance to certain β-lactam, aminoglycoside and macrolide antibiotics. An example of this may be pneumonia, which the World Health Organization has identified as one of the six diseases that account for over 90% of all human illnesses. Pneumonia belongs to acute respiratory infections, causing bacteria Streptococcus pneumoniae, and if not treated, it can cause death very quickly. Although, benzylpenicillin has been used as medication choice for pneumonia, today it is known that certain strains of the bacteria developed high resistance rates for erythromycin, trimethoprim-sulfamethoxazole, and tetracycline, which reduced the number of drugs in the treatment (1).

Given the development of resistance to antimicrobial therapy and the emergence of new pathogenic strains, there is a permanent need to find new pharmacologically active substances that will be used to prevent and/or treat people and animals. The development of new drugs is a long-lasting and costly process, and in order to rationalize the time and money spent on finding and synthesizing new drugs, rational drug design is often use. Also, attention is paid to isolation and semi-synthetic production of compounds from natural materials. One such group of compounds are xanthane compounds whose pharmacological use has been known since the '70s of the last century. In 1968, Bhattacharya described the diuretic and cardiac effects of natural glycosides of mangiferin (2).

1. Structure of Xanthene

A large number of xanthene compounds have a wide opus of action on human and animal organisms. The pyranic ring has main responsibility for it (Figure 1), which can react with other substrates, where xanthene derivatives are formed as products. The most prominent among them are xanthones.

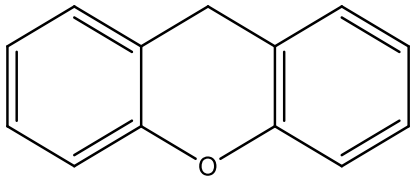

Figure 1. Structure of xanthene.
Şekil 1. Ksantenin yapısı.

The Xanthones isolated so far may be classified into five major groups: simple oxygenated xanthones, xanthones glycosides, prenylated xanthones, xanthonolignoids and miscellaneous.

Simple oxygenated xanthones are subdivided according to the degree of oxygenation into non-, mono-, di-, tri-, tetra-, penta-, and hexaoxygenated substances.

Xanthones gycosides can be classified into C-glycosides and O-glycosides. In C-glycosides, C–C bond links the sugar moiety to the xanthone nucleus and they are resistant to acidic and enzymatic hydrolysis whereas the O-glycosides have typical glycosidic linkage. Mangiferin and isomangiferin are the most common C-glycosides, while first O

glycoside was norswertianin-1-O-glucosyl-3-O-glucoside isolated from *S. perennis*.

The occurrence of prenylated xanthones is restricted to the plant species of the family Guttiferae. The major C5 unit of the substituents included the commonly found 3-methylbut-2-enyl or isoprenyl group as in isoemericellin and the less frequent 3-hydroxy-3-methylbutyl as in nigrolineaxanthone P. The most important prenylated xanthones are caloxanthone O and caloxanthone P, wich were isolated from Calophyllum inophyllum.

Naturally occurring xanthonolignoids are rare, so only five compounds are known. The most important are cadensin C and cadensin D from Vismia guaramirangae and Hypericum canariensis, Cadensins A and B from Caraipa densiflora.

Xanthones with substituents other than those mentioned above are included in miscellaneous group. Xanthofulvin and vinaxanthone are the most important in this class and were isolated from *Penicillium* species (3).

Xanthen derivatives exhibit various pharmacological effects such as antibacterial, antifungal (4), antihelmintic, antiallergic (5), antiprotozoal, antioxidant (6), gastroprotective (7) and antidiabetic (8). Also, xanthones possess an antidepressant action and an antitubercular activity, while xanthone glycosides have a depressive action. A choleretic, diuretic, antimicrobial, antiviral and cardiotonic action of some xanthones has also been established. The inhibition of Type A and Type B monoamine oxidases by a number of xanthones have also been observed (9).

The latest study (10) indicates that xanthene derivatives do not have genotoxic activity at the tested concentrations, but had good antiproliferative effect, which is another reason for their further examination.

2. Antibacterial Effect of Xanthene Compounds

A large number of published papers describe the antibacterial activity of natural or synthetic xanthenes or its derivatives.

Tantapakul et al. (11) examined the effect of xanthen isolated from the plant *Cratoxylum sumatranum* ssp. neriifolium to Gram positive *Micrococcus luteus*, *Bacillus cereus*, *Bacillus subtilis*, *Staphylococcus aureus* and *Staphylococcus epidermidis* and Gram negative *Escherichia coli*, *Salmonella typhimurium* and *Pseudomonas aeruginosa* bacteria and they came to the conclusion that some isolated xanthen derivatives show good antimicrobial effects on *M. luteus*, *B. cereus*, *S. epidermis* with minimal inhibitory concentration (MIC) 4-8µg/ml and on *P. aeruginosa* MIC 4 µg/ml, *S. aureus* MIC 8 µg/ml and *S. Typhimurium* MIC 4 µg/ml.

In Stoil's study et al. (12) it has been proved in vitro effect of mangiferin (Figure 2), xanthene isolated from the plant *Mangifera indica* L. on *Bacillus pumilus*, *Bacillus cereus*, *Staphylococcus aureus*, *Staphylococcus citreus*, *Escherichia coli*, *Salmonella agona*, *Klebsiella pneumoniae* and *Saccharomyces cerevisiae*, whereby it was observed that the less concentrations of mangiferin till 20%, solutions prepared in polyethylene glycol-400, were necessary for inhibiting Gram positive bacteria. The most sensitive strain was B. pumilus, while slightly more concentration was required to inhibit Gram negative bacteria (30 till 35%), and the most sensitive strain was S. agona. In any of the tested concentrations 8-35%, mangiferin didn't show activity on *P. aeruginosa*.

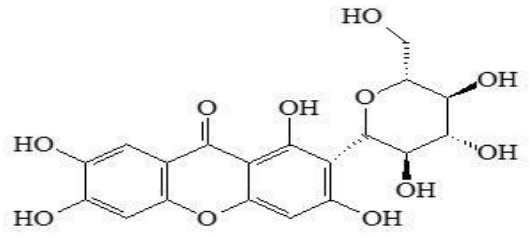

Figure 2. Structure of Mangiferin.
Şekil 2. Magniferinin yapısı.

One of the most widespread hospital infections is the meticillin-resistant type *Staphylococcus aureus* MRSA. Studies have shown that xanthones α-mangostin and rubraxantone, isolated from some plants of the Guttiferae family show good activity on this form of the bacteria (13). Thus, isolated α-mangostin had MIC 1.57-12.5 μg/ml, while rubraxantone had MIC 0.31-1.25 μg/ml, which is even better than the vancomycin antibiotic that had MIC 3.13-6.25 μg/ml.

The activity of α-mangostin and β-mangostin, xanthones isolated from the *Garcinia mangostana* plant L. on MRSA was also examined in the study Sakagami et al. (14). Also, there were examinated effects of these xanthones in combination with commercially available antibiotics, ampicillin, gentamicin, minocycline and vancomycin hydrochloride. Results showed that α-mangostin, individually and in combination with vancomycin hydrochloride, has an extremely good effect on MRSA.

Tuberculosis, a disease caused by bacteria *Mycobacterium tuberculosis* is the cause of millions of deaths worldwide, although for many years there has been approved therapy and vaccination. In the study Szkaradek et al. (15) newly synthesized 2-xanthone derivatives, 2-2-4-2-4-chloro-3-methylphenoxy) ethyl) piperazin-1-yl) ethoksy)-9H-xanthen-9-one, 2-4-2-4-chlor-3-methylphenoxy) ethyl) piperazin-1-yl) methyl)-9H-xanthen-9-one dihydrochloride and ethyl 4-2-hydroxy-3-9-oxo-9H-xanthen-2-yloxi) propyl piperazine carboxylate, have shown inhibitory effects on *Mycobacterium tuberculosis*, but they also had a cytotoxic effect.

Recent studies of natural xanthones have shown that α-mangostin have good activity according to *Mycobacterium tuberculosis* with MIC from 62 μg/mL (16), while in study Sudta et al. (17) it has been shown that monoalkyl tetrahydro-α-mangostin analogs show an even better antibacterial effect than α-mangostin alone. Best results had 6-methoxytetrahydro-α-mangostin with MIC 0,78 μg/mL.

Study Veljovic et al. (18) describe antimicrobial activity of new synthesized xanthen-3-on derivates in vitro against *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Escherichia coli*. The results showed that all derivates have good antimicrobial activity, but those with bromine and hydroxyl group in structure had stronger antimicrobial activity. Also, one more study (19) showed that some of new xanthen derivates have very good antimicrobial effect on *Escherichia coli* and *Staphylococcus aureus*, so it is clearly that this is a field to work on it.

The exact mechanism of action of xanthene derivatives is still unknown, but it is thought that they exert their activity by some of the following mechanisms: tree lignification, enzyme inhibition, phosphodiester reactions, alkylation and DNA cross-linking (20).

3. Antihelmintic Effect of Xanthene Compounds

Ecto and endo parasites in veterinary medicine represent a significant problem, adversely affecting the health of animals, and contributing to significant material losses in livestock production. All domesticated animals, including pets and laboratory animals, are subject to a large number of different parasitosis. The survivors of intensive farm breeding, in controlled conditions of nutrition and keeping, are minimally exposed to ecto and endo parasite infestations. The same applies to pets and laboratory animals. However, ruminants with an extensive way of keeping throughout the grazing season, from early spring to late autumn, are exposed to infections of various types of parasites daily, ranging from flat worms big and small mites, ribbons, echinococcus and round worms pulmonary and intestinal strongylides, etc. to ticks and insects ixodides, acars, flakes and other.

As a result of the infection of animals, there are large losses in the livestock industry. Specifically, large amounts of internal organs are discarded in slaughter (21).

In a retrospective four-year study of the parasites of the mountain-mountain regions of Bosnia and Herzegovina, complete parasitology sections have been examined 5.805 rats, and a positive finding was found in 5084 animals or 87.6%. The obtained results indicate that the highest incidence is at sheep, during the entire period of the study, was related to dicrocelia, among others, to cattle on fasciolosis and paramfistomosis (22). These facts support the fact that the possible use of natural or synthetic xanthene compounds that exhibit antihelmintic activity has made significant benefits in veterinary curative.

In study Keiser's et al. (23) was examined the effect of natural xanthen, mangostin, isolated from the plant *Garcinia mangostana* and its synthetic derivative, mangostin diacetate on nematodes *Heligmosomoides polygyrus*, *Ancylostoma ceylanicum*, *Trichuris muris* and trematode *Schistosoma mansoni*, *Echinostoma caproni*, *Fasciola hepatica*. Both compounds did not show positive effects, except for exceptionally poor activity on *A. ceylaniucum*. On trematodes, mangostin showed very poor performance, while mangostin diacetate had a slightly better effect on *S. mansoni* i *E. caproni*.

Ondeyka et al. (24) examined the action of xanthol (Figure 3) and confirmed its insecticidal and antihelmintic effect on *Aedes aegypti*, *Lucilia sericata* i *Haemonchus contortus*.

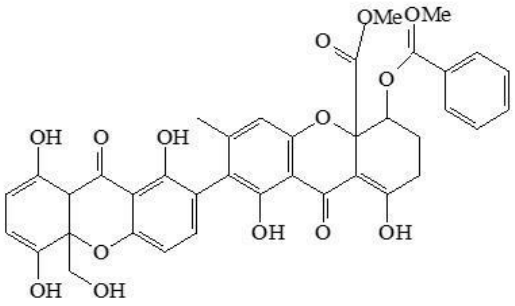

Figure 3. Structure of Xanthol.
Şekil 3. Ksantolun yapısı.

More frequent occurrence of zoonosis caused by infection *Opisthorchis viverrini* in the area of Southeast Asia is a major problem. In humans, infection occurs after the consumption of raw fish that is contaminated with larvae of said trematode. As a result of the infection, various liver diseases such as hepatitis, cholangitis and cancer occur in animals.

Aukkanimart R. et al. (25) examined the effect of xanthenes isolated from the plant *Garcinia mangostana* on the indicated trematode and found that in addition to antiinflammatory and antioxidant action, the extract can be effective in controlling the spread of the infection caused by *Opisthorchis viverrini*. In experimental animals infected with this trematode and treated with extract of the plant, it was observed that the growth of reproductive organs was inhibited, resulting in a decrease in the number of parasite eggs.

Xanthene derivatives show anthelmintic activity. It is still unclear, but it is considered that they possess this activity through inhibiting microtubule synthesis in nematodes, thus irreversibly impairing glucose uptake. As a result, intestinal parasites are immobilized or die slowly (26).

4. Antiprotozoal Activity

Malaria is a disease caused by four types *Plasmodium*: *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*. Xanthones represent potential antimalarials. Garciniaxanthon B (Figure 4), isolated from the plant species *Garcinia subelliptica*, shows very good activity towards *Trypanosoma cruzi*.

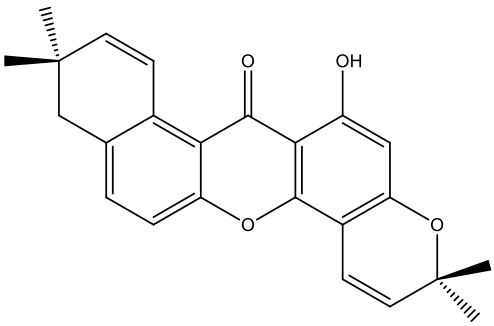

Figure 4. Structure of Garciniaxanthon B.
Şekil 4. Garsiniaksanton B'nin yapısı.

Hydroxyxanthones have been identified as the new antimalarial agents. It is believed that this

activity is expressed by complexing the HEM and inhibiting the formation of hemosins (27,28).

In 1986, Ampofo isolated dimethylcalabaxanthone and calotvaitesixantone from Calophyllum caledonicum species. It is believed that these two xanthonic derivatives exhibit their antimalarial activity due to the position of the hydroxyl groups on the xanthone core, the presence of the piran cycle and the dimethylalyl chain. (29)

Riscoe synthesized 3,6-bisω-N,N-dietilaminoamiloksi)-4,5-difluoroksanton (F2C5) (Figure 5) which showed good activity towards resistant strains *Plasmodium falciparum* (30). The existence of xanthone structure is the most important for antimalarial activity. It is believed that the carbonyl bridge coordinates with iron in the structure of the heme. Also, the aromatic rings F2C5 react with the aromatic rings of the heme, so that this xanthone exhibits its antimalarial activity by interfering with the structure of the heme that is important for the life cycle *Plasmodium falciparum* (31,32).

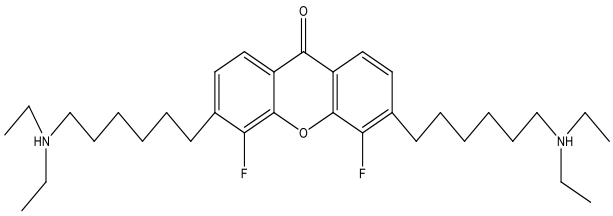

Figure 5. Structure of 3,6-bis (ω-N,N-dietilaminoamiloxy]-4,5-difluoroxanthon (F 2 C 5).
Şekil 5. 3,6-bis (ω-N,N-dietilaminoamiloxy]-4,5-difluoroxanthon (F 2 C 5)'nın yapısı.

The exact mechanism by which xanthene derivatives exert an antiprotozoal effect is still unknown, it is considered that they thought the inhibit the enzyme trypanothione reductase they stop the growth and further replication of the protozoa (33).

5. Antifungal Activity

Although bacterial and viral infections are more common, fungal infections do not have the same characteristics. This is especially expressed in people with immunodeficiency, whether it is primary or secondary, so that the search for new compounds with antifungal activity is constant.

Fukai et al. (34) examined the effects of xanthene derivatives isolated from the plant *Cudrania cochinchinensis* on *Candida*, *Cryptococcus* and *Aspergillus* types of fungus. Results of the study have shown that cudraxantone S and toxyloxanthone C (Figure 6) show antifungal activity against fungi *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Aspergillus nidulans* and *Candida glabrata*.

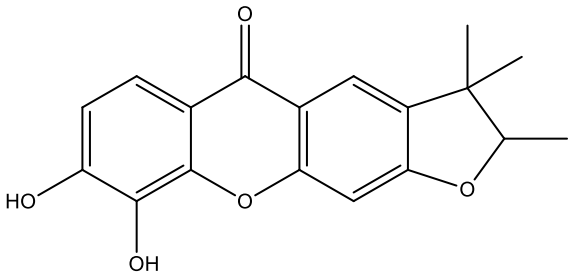

Figure 6. Structure of Toxyloxanthone C.
Şekil 6. Toksiloksanton C'nin yapısı.

Best antifungal effect according to *Candida albicans* species has toxyloxanthone C isolated from *Cudrana fruticosa* with minimal inhibitory concentration 25 μg/ml (35).

Marona et al. (4) synthesized 20 new 2-substituted xanthones, and then tested their antifungal action in vitro against *Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida lusitaniae*, *Cryptococcus neoformans* and *Trichophyton mentagrophytes*. Ten newly synthesized derivatives showed antifungal activity according *to Trichophyton mentagrophytes*, with a maximum inhibition band of 35mm, while it 2-3-allylaminopropoxy-9H-xanthen-9-one hydrochloride acted on all examinated strains of fungi.

CONCLUSION

In literature are described a various pharamcological effects of xanthene derivatives.

Sometimes, at certain concentrations, xanthenes show resistance to some microbes, but that does not mean that at other concentrations they cannot show a positive effect, which also indicates

the need for new synthesis of xanthene derivatives, as well as further studies on other pharmacological effects.

This would give a more insight into the effectiveness of xanthen derivatives in human and veterinary medicine.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Cai K., Wang Y., Guo Z., Xu X., Li H., Zhang Q., 2018. Clinical characteristics and antimicrobial resistance of pneumococcal isolates of pediatric invasive pneumococcal disease in China. Infect Drug Resist, 11, 2461-2469.
2. Fotie J., Bohle DS., 2006. Pharmacological and biological activities of xanthones. Anti-Infect Agent Med Chem, 5, 15-31.
3. Negi JS., Bisht VK., Singh P., Rawat MSM., Joshi GP., 2013. Naturally occurring canthones: chemistry and biology. J App Chem, 1, 1-9.
4. Marona H., Szkaradek N., Karczewska E., Trojanowska D., Budak A., Bober P., Przepiorka W., Cegla M., Szneler E., 2009. Antifungal and Antibacterial Activity of the Newly Synthesized 2-Xanthone Derivates. Arch Pharm (Weinheim), 342, 9-18.
5. Garcia D., Escalante M., Delgado R., Ubeira FM., Leiro J., 2003. Anthelminthic and antiallergic activities of Mangifera indica L. stem bark components Vimang and mangiferin. Phytother Res, 17, 1203-1208.
6. Veljovic E., Spirtovic-Halilovic S., Muratovic S., Valek Zulj L., Roca S., Trifunovic S., Osmanovic A., Davorka Z., 2015. 9-Aryl substituted hydroxylated xanthen-3-ones: Synthesis, structure and antioxidant potency evaluation. Croat Chem Acta, 88, 121-127.
7. Mariano LN., Da Silva LM., De Souza P., Boeing T., Somensi LB., Bonomini TJ., Delle Monache F., Cechinel Filho V., de Andrade SF., Niero R., 2016. Gastroprotective xanthones isolated from Garcinia achachairu: Study on mucosal defensive factors and H (+), K(+)-ATPase activity. Chem Biol Interact, 258, 30-39.
8. Irondi EA., Oboh G., Akindahunsi AA., 2016. Antidiabetic effects of Mangifera indica Kernel Flour-supplemented diet in streptozotocin-induced type 2 diabetes in rats. Food Sci Nutr, 4, 828-839.
9. Peres V., Nagem TJ., 1997. Naturally occurring, pentaoxygenated, hexaoxygenated and dimeric xanthones: A literature survey. Quimica Nova, 20, 388-397.
10. Veljovic E., Spirtovic-Halilovic S., Muratovic S., Osmanovic A., Haveric S., Haveric A., Hadzic M., Salihovic M., Malenica M., Sapcanin A., Zavrsnik D., 2019. Antiproliferative and genotoxic potential of xanthen-3-one derivatives. Acta Pharm, 69, 683-694.
11. Tantapakul C., Maneerat W., Sripisut T., Ritthiwigrom T., Andersen RJ., Cheng P., Cheenpracha S., Raksat A., Laphookhieo S., 2016. New Benzophenones and Xanthones from Cratoxylum sumatranum ssp. neriifolium and Their Antibacterial and Antioxidant Activities. J Agric Food Chem, 64, 8755-8762.
12. Stoilova I., Gargova S., Stoyanova A., Ho I., 2005. Antimicrobial and antioxidant activity of the polyphenol mangiferin. Herba Polonica, 51, 1-2.
13. Iinuma M., Tosa H., Tanaka T., Asai F., Kobayashi Y., Shimano R., Miyauchi K., 1996. Antibacterial activity of xanthones from guttiferaeous plants against methicillin-resistant Staphylococcus aureus. Pharm Pharmacol, 48, 861-865.
14. Sakagami Y., Iinuma M., Piyasena KG., Dharmaratne HR., 2005. Antibacterial activity of alpha-mangostin against vancomycin resistant Enterococci (VRE) and synergism with antibiotics. Phytomedicine, 12, 203-208.
15. Szkaradek N., Stachura K., Waszkielewicz AM., Cegla M., Szneler E., Marona H., 2008. Synthesis and antimycobacterial assay of some xanthone derivatives. Acta Polon pharm, 65, 21-28.

16. Guzman-Beltran S., Rubio-Badillo MA., Juarez E., Hernandez-Sanchez F., Torres M., 2016. Nordihydroguaiaretic acid (NDGA) and α-mangostin inhibit the growth of Mycobacterium tuberculosis by inducing autophagy. Int Immunopharm, 31, 149-157.
17. Sudta P., Jiarawapi P., Suksamrarn A., Hongmanee P., Suksamrarn S., 2013. Potent activity against multidrug-resistant Mycobacterium tuberculosis of α-mangostin analogs. Chem Pharm Bull, 61, 194-203.
18. Veljovic E., Spirtovic-Halilovic S., Muratovic S., Salihovic M., Novakovic I., Osmanovic A., Zavrsnik D., 2018. Antimicrobial activity and docking study of synthesized xanthen-3-on derivatives. RJPBCS, 9, 777-783.
19. Veljovic E., Spirtovic-Halilovic S., Kahrovic E., Roca S., Novakovic I., Osmanovic A., Salihovic M., Alagic D., Benjamin H., Dzenana L., Zavrsnik D., 2016. Solvent-free Synthesis and Antibacterial Activity of 14-Aryl Substituted Dibenzoxanthene Derivatives. Bull Chem Tech Bosnia and Herzegovina, 46, 33-38.
20. Futuro DO., Ferreira PG., Nicoletti CD., Borbasantos LP., Da Silva F., Rozental S., Ferreira VF., 2018. The antifungal activity of naphthoquinones: An integrative review. Ann Acad Bras Cienc, 1, 90.
21. Moro P. and Schantz M.P., 2009. Echinococcosis: a review. International Journal of Infectious Diseases, 13, 125-133.
22. Zuko A., 1999. Parasites and parasitoses in ruminants in the upland regions in Bosnia and Herzegovina. Veterinaria, 48, 95-120.
23. Keiser J., Vargas M., Winter R., 2012. Anthelminthic properties of mangostin and mangostin diacetate. Parasitol Int, 61, 369-371.
24. Ondeyka JG., Dombrowski AW., Polishook JP., Felcetto T., Shoop WL., Guan Z., Singh SB., 2006. Isolation and insecticidal/anthelmintic activity of xanthonol, a novel bis-xanthone, from a Non-sporulating fungal species. J Antibiotics, 59, 288-292.
25. Aukkanimart R., Boonmars T., Sriraj P., Songsri J., Laummaunwai P., Waraasawapati S., Boonyarat C., Rattanasuwan P., Boonjaraspinyo S., 2015. Anthelmintic, anti-inflammatory and antioxidant effects of Garcinia mangostana extract in hamster opisthorchiasis. Exp Parasitol, 154, 5-13.
26. Garcia-Bustos JF., Sleebs BE., Gasser RB., 2019. An appraisal of natural products active against parasitic nematodes of animals. Parasit Vectors, 12, 306.
27. Scott H., Ralf W., 2007. One-pot synthesis of new symmetric and asymmetric xanthene dyes. Tetrahedron Lett, 48, 4383-4385.
28. Shao-liang Z., Philp C., 2005 Synthesis, structures, photoluminescence and theoretical studies of xanthone in crystalline resorcinarene-based inclusion complexes. Chem Eur J, 11, 3583-3590.
29. Sousa E., Correia da Silva M., Pinto M., 2009. In: Natural Products Chemistry, Biochemistry and Pharmacology, Ed., Narosa Publishing House PVT. LTD., 392-416, West Bengal, India.
30. Eunice MT., 2006. Antiprotozoal activity against plasmodium falciparum and trypanosoma cruzi of xanthones isolated from chrysochlamys tenuis. Pharm Biol, 7, 550-553.
31. Fotie J., Bohle S., 2006. Pharmacological and biological activities of xanthones. Curr Med Chem-Anti-Infect Agents, 5, 15-31.
32. Pinto M., Castanheiro R., 2009. In: Natural Products Chemistry, Biochemistry and Pharmacology, Ed., Narosa Publishing House PVT. LTD., 520-675, West Bengal, India.
33. Kaiser M., Maser P., Tadoori LP., Loset JR., Brun R., 2015. Antiprotozoal activity profiling of approved drugs: A starting point toward drug repositioning. PLOS ONE, 10, 8.
34. Fukai T., Yonekawa M., Hou AJ., Nomura T., Sun HD., Uno J., 2003. Antifungal agents from the roots of Cudrania cochinchinensis against Candida, Cryptococcus, and Aspergillus species. J Nat Prod, 66, 1118-1120.
35. Jean F., Scott B., 2003. Pharmacological activities of xanthones. Anti-Inf Agents in Med Chem, 3, 11-17.