# ESTIMATIONS OF ANTIBACTERIAL ACTIVITY OF MODIFIED THIO-NUCLEOSIDES

# ОЦЕНКА АНТИБАКТЕРИАЛЬНОЙ АКТИВНОСТИ МОДИФИЦИРОВАННЫХ ТИОНУКЛЕОЗИДОВ

***S . R. Albasri, A. G. Sysa***

***С. Р. Альбасри, А. Г. Сыса***

*International Sakharov Environmental Institute of Belarusian State University, ISEI BSU*
*Minsk, Republic of Belarus*
*yuridragonv@gmail.com*
*Учреждение образования «Международный государственный экологический институт имени А. Д. Сахарова» Белорусского государственного университета, МГЭИ им. А. Д. Сахарова БГУ*
*Минск, Республика Беларусь*

Foodborne disorders are sicknesses or illnesses that arise in an individual after they have ingested debased food or water. This contamination is occasionally the outcome of corrupting with pathogenic minute organic entities, some of which can cause affliction through the improvement of enterotoxins [1]. These foodborne ailments every now and again present with self-confining gastroenteritis aftereffects i.e., affliction, regurgitating, detachment of the entrails, stomach issues, and fever, but outrageous complexities can moreover arise, similar to kidney and liver dissatisfaction, psyche and cerebrum issues, and loss of movement, which can have deadly outcomes. The World Health Organization assesses the yearly weight of foodborne disease to number 600 million instances of sickness universally; of this, diarrheal ailment represents the biggest extent of these cases and results in 230,000 passing [1]. These numbers, be that as it may, are reasonable underrates because of a scope of elements including non-compulsory revealing of cases to fitting reconnaissance frameworks, absence of worldwide observation frameworks, absence of properly prepared testing offices, as well as that those experiencing gentle side effects may not look for clinical consideration [1-3]. The investigation of infection transmission of foodborne sickness is huge for the early acknowledgment of emerging examples. With the globalization of food supply chains, it is basic to not simply have some familiarity with the investigation of sickness transmission of foodborne disease, yet furthermore of the causative experts captured in these.

Расстройства пищевого происхождения – это заболевания или недомогания, которые возникают у человека после употребления в пищу испорченной пищи или воды. Это загрязнение иногда является результатом заражения мелкими патогенными органическими веществами, некоторые из которых могут вызывать заболевания за счет содержания энтеротоксинов [1]. Эти заболевания пищевого происхождения время от времени сопровождаются самопротекающими последствиями гастроэнтерита, т. е. недомоганием, срыгиванием, отслоением внутренностей, проблемами с желудком и лихорадкой, но, кроме того, могут возникать возмутительные сложности, подобные неудовлетворенности почек и печени, проблемам с психикой и мозгом. и потеря движения, что может иметь смертельные последствия. По оценкам Всемирной организации здравоохранения, ежегодный вес болезней пищевого происхождения насчитывает 600 миллионов случаев заболеваний во всем мире; из них диарейное заболевание представляет собой наибольшую распространенность этих случаев и приводит к смерти 230 000 человек [1]. Эти цифры, как бы то ни было, разумно занижены из-за множества элементов, включая необязательное выявление случаев с помощью соответствующих систем разведки, отсутствие всемирных систем наблюдения, отсутствие должным образом подготовленных офисов тестирования, а также побочные эффекты могут не требовать клинического рассмотрения [1-3]. Расследование передачи инфекций пищевого происхождения имеет огромное значение для раннего выявления новых примеров. В условиях глобализации цепочек поставок продовольствия крайне важно не просто иметь некоторое представление о расследовании случаев передачи болезней пищевого происхождения, но, кроме того, о привлеченных к ним экспертах.

*Keywords:* antibacterial drugs, modified nucleosides, DNA replication enzymes, antimetabolites,

*Ключевые слова:* антибактериальные препараты: докинг, модифицированные нуклеозиды, ферменты репликации ДНК, антиметаболиты.

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*Bacillus cereus* species and Staphylococcus aureus are among the most huge enterotoxigenic foodborne microorganisms. These bacterial species produce different enterotoxins that have been entangled in various cases of foodborne ailment, generally causing either emetic or diarrheal secondary effects.

*B. cereus*, an individual from the *B. cereus* bunch (*B. cereus* (sensu stricto), B. weihenstephanensis, B. thuringiensis, B. mycoides, B. pseudomycoides, B. anthracis, B. cytotoxicus and B. toyonensis), is a Gram-positive spore framing

bacterium. They can convey different enterotoxins including non-hemolytic enterotoxin (NHE), hemolysin BL (HBL), cytokine K (CytK), hemolysin II (HlyII), enterotoxin FM (EntFM), and enterotoxin T (bc-D-ENT). As spore-formers they can acquaint an extended bet with food taking care of since spores could get through dealing with controls in food taking care of, similar to sterilization.

*S. aureus* is a Gram-positive non-spore forming coccus and strains could have a colossal assortment of enterotoxins, as reviewed by Argudin et al.. This consolidates more than 23 power stable staphylococcal enterotoxins (SEs) including Sea to SEE, SEG to SEI, SEK to SET, and the staphylococcal enterotoxin-like proteins (SEls) SElJ, and SElU-SElY [15]. Sea to SEE are seen as the 'customary' enterotoxins and have all been trapped in foodborne sickness cases. SEH is the primary non-old style enterotoxin that has moreover been entrapped in causing disorder episodes.

Gastroenteric contamination brought about by B. cereus s. l. species or S. aureus is believed to be only through ingestion of debased food varieties. To this end, look for novel mixtures that might have antibacterial movement, as well as the comprehension of the sub-atomic instruments behind these mixtures' activities, are of essential and functional importance.

Perhaps of the main pharmacological class utilized in clinical practice is adjusted nucleosides, which are generally utilized as antiviral and anticancer specialists [1]. Be that as it may, data about their productivity against microorganisms has been gathering as of late. As of now, nucleosides' antibacterial properties have been found in both their engineered analogs and various normal substances [19-21]. Furthermore, perceived nucleosides that have been or alternately are currently being used to treat different infections have been uncovered to have antimicrobial attributes [2].

In this study the antibacterial activity of modified thio-nitrogen bases 2-mercaptopurine and 6-thioguanine, as well as thio-nucleosides 6-thioguanosine and 2'-deoxy-6-thioguanosine against *S. aureus* and *B. cereus* were studied.

*Different convergences of the adjusted nitrogen bases 2-mercaptopurine, 6-thioguanine, and nucleosides 6-thioguanosine and 2'-deoxy-6-thioguanosine are assessed for their impact on the viability of opportunistic gram-positive bacterial cultures of B. cereus and S. aureus.*

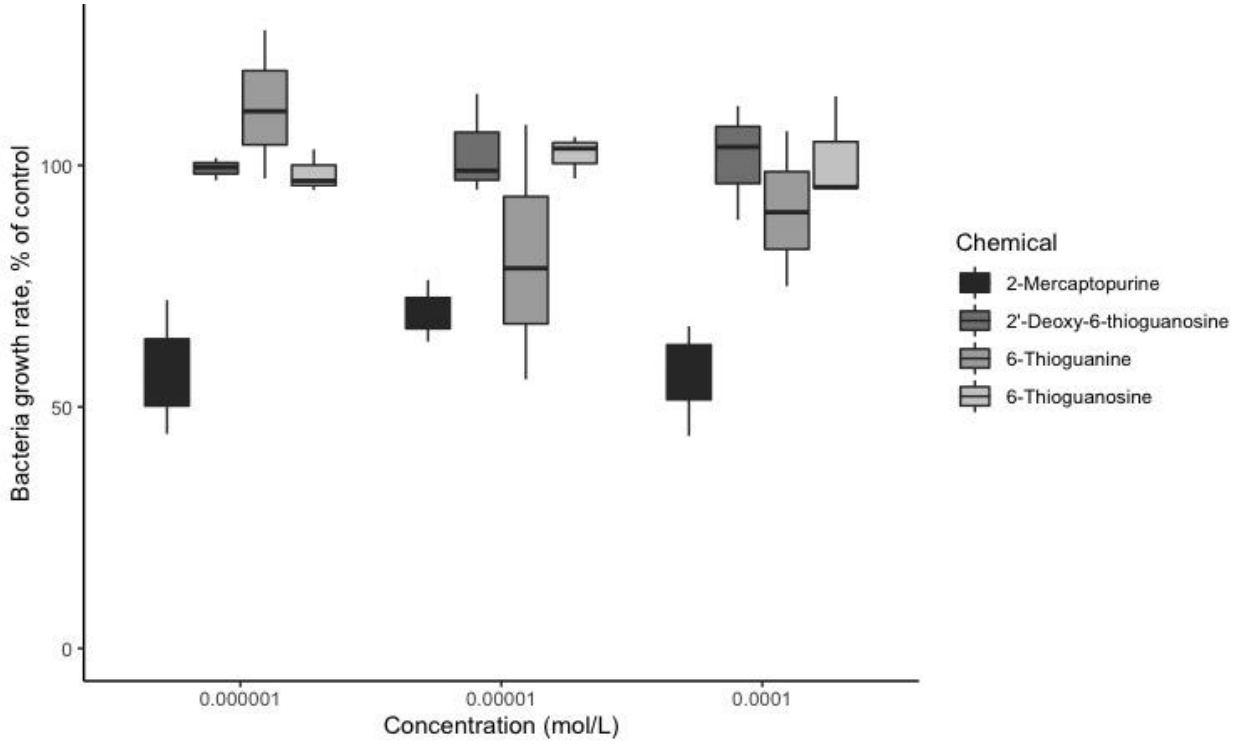


*Figure 1 – Effects of different concentrations of 2-mercaptopurine, 6-thioguanine, 6-thioguanosine, and 2'-deoxy-6-thioguanosine on the growth of B. cereus bacterial cells*

According to the data shown in Figure 2, only 2-mercaptopurine had a visible effect on B. cereus bacterial cells growth. Indeed, the median bacteria growth rate after 2-mercaptopurine treatment was 63.5% (IQR = 12.9), whereas the median in 6-thioguanine-treated group was 97.3% (IQR = 29.7).

In nucleosides-treated groups more homogenous data were got. In 6-thioguanosine-treated group the median was similar to 6-thioguanine-treated group 97.3% (IQR = 8.0), whereas the median bacteria growth rate after 2'-deoxy-6-thioguanosine treatment was 99.6% (IQR = 6.9).

The Kruskal-Wallis test displayed that the differences were substantial (p = 0.0005365, Kruskal-Wallis chi-squared = 17.581).

Next pairwise examinations between bunch levels with rectifications for various testing were determined (Table).

Table

*Pairwise comparisons of the effect of different concentrations of 2-mercaptopurine, 6-thioguanine, 6-thioguanosine, and 2'-deoxy-6-thioguanosine on the viability of B. cereus bacterial cells using Wilcoxon rank sum test results*

| Compound | 2-Mercaptopurine | 2'-Deoxy-6-thioguanosine | 6-Thioguanine |
|---|---|---|---|
| 2'-Deoxy-6-thioguanosine | 0.00012 | - | - |
| 6-Thioguanine | 0.00551 | 0.82519 | - |
| 6-Thioguanosine | 0.00012 | 0.82519 | 0.82519 |

The pairwise comparison shows that, only 2-mercaptopurine and other compounds are significantly different ($p < 0.05$), whereas 6-thioguanosine pairwise with 6-thioguanine, and 2'-deoxy-6-thioguanosine, as well as 6-thioguanine pairwise with 2'-deoxy-6-thioguanosine were similar in its effects on growth of *B. cereus* cells ($p = 0.82519$).

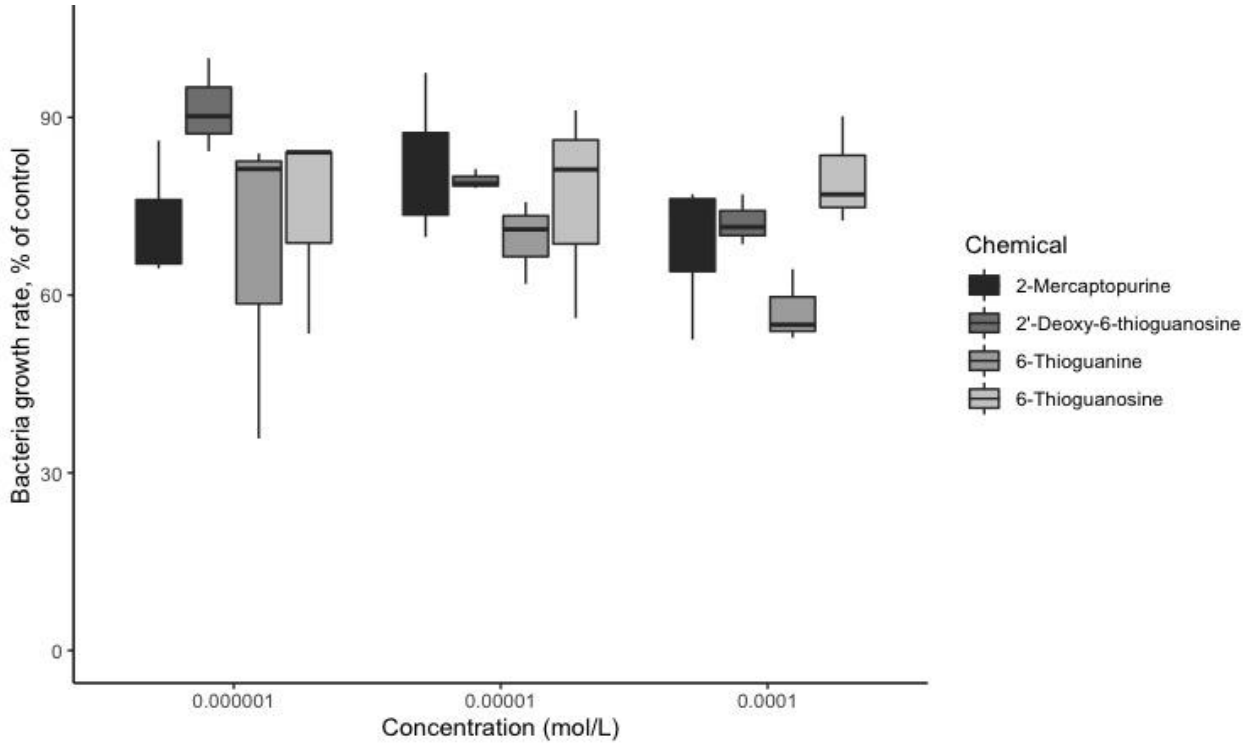


*Figure 2 – Effects of different concentrations of 2-mercaptopurine, 6-thioguanine, 6-thioguanosine, and 2'-deoxy-6-thioguanosine on the growth of S. aureus bacterial cells*

According to the data shown in Figure 2, all compounds showed the effect on growth of *S. aureus* bacterial cells. 6-Thioguanine was the most active nitrogen base with the median bacteria growth rate 64.4% (IQR = 20.7), moreover, this compound was the only one showed a concentration dependent effect on cell growth.

The median in 2-mercaptopurine-treated group was 75.5% (IQR = 11.2). In nucleosides-treated groups the median was 78.8% (IQR = 7.3) in 2'-deoxy-6-thioguanosine-treated group, and 81.2% (IQR = 11.6) in 6-thioguanosine-treated group.

The performed Kruskal-Wallis test displayed that there were no major differences among compounds ($p = 0.08845$, Kruskal-Wallis chi-squared = 6.5311).

This study constantly demonstrated that 6-thioguanine, 6-thioguanosine, and 2'-deoxy-6-thioguanosine, but not 2-mercaptopurine treatment on *B. cereus* bacterial cells via resazurin reduction assay for 24 hours did not produce any significant toxic effects. The results in this study also demonstrated that studied modified nitrogen bases 2-mercaptopurine, 6-thioguanine, and nucleosides 6-thioguanosine and 2'-deoxy-6-thioguanosine were more significant decreased the growth of *S. aureus* bacterial cells with concentration dependent manner in case of 6-thioguanine.

## REFERENCES

1. WHO . *WHO Estimates of the Global Burden of Foodborne Diseases.* World Health Organization; Geneva, Switzerland: 2015. p. 268.

2. Buzby J.C., Roberts T. The Economics of Enteric Infections: Human Foodborne Disease Costs. *Gastroenterology.* 2009;136:1851–1862. doi: 10.1053/j.gastro.2009.01.074.

3. Flint J.A., Van Duynhoven Y.T., Angulo F.J., DeLong S.M., Braun P., Kirk M., Scallan E., Fitzgerald M., Adak G.K., Sockett P., et al. Estimating the Burden of Acute Gastroenteritis, Foodborne Disease, and Pathogens Commonly Transmitted by Food: An International Review. *Clin. Infect. Dis.* 2005;41:698–704. doi: 10.1086/432064.

4. Delbrassinne L., Botteldoorn N., Andjelkovic M., Dierick K., Denayer S. An Emetic *Bacillus cereus* Outbreak in a Kindergarten: Detection and Quantification of Critical Levels of Cereulide Toxin. *Foodborne Pathog. Dis.* 2014;12:84–87. doi: 10.1089/fpd.2014.1788.

5. Fetsch A., Contzen M., Hartelt K., Kleiser A., Maassen S., Rau J., Kraushaar B., Layer F., Strommenger B. Staphylococcus aureus food-poisoning outbreak associated with the consumption of ice-cream. *Int. J. Food Microbiol.* 2014;187:1–6. doi: 10.1016/j.ijfoodmicro.2014.06.017.

# ESTIMATIONS OF CANCER CELLS ACTIVITY USING MODIFIED THIO-NUCLEOSIDES

# ОЦЕНКА АКТИВНОСТИ РАКОВЫХ КЛЕТОК С ПОМОЩЬЮ МОДИФИЦИРОВАННЫХ ТИО-НУКЛЕОЗИДОВ

***S. R. Albasri, A. G. Sysa***

***С. Р. Альбасри, А. Г. Сыса***

*International Sakharov Environmental Institute of Belarusian State University, ISEI BSU*
*Minsk, Republic of Belarus*
*yuridragonv@gmail.com*
*Учреждение образования «Международный государственный экологический институт имени А. Д. Сахарова» Белорусского государственного университета, МГЭИ им. А. Д. Сахарова БГУ*
*Минск, Республика Беларусь*

Thio-nucleosides, a group of chemicals generated from nucleosides by replacing the oxygen atom with a sulfur atom, have received a lot of attention in cancer research because of their potential anticancer effects. Thio-nucleosides' unusual chemical structure confers specific biological activity, making them possible cancer therapeutic possibilities. This article will look at the role of thio-nucleosides as anticancer medications and how they work to limit cancer cell growth and induce apoptosis. Thio-nucleosides have demonstrated exceptional cytotoxic effects on a variety of cancer cell lines, making them a promising target for future preclinical and clinical research. Their capacity to interfere with nucleic acid metabolism and impair DNA replication and repair mechanisms in cancer cells has made them viable chemotherapeutic agents. Furthermore, thio-nucleosides have demonstrated the ability to overcome drug resistance, a significant obstacle in cancer treatment, opening up new pathways for the creation of effective anticancer medicines. In this article, we will look at the molecular processes underpinning thio-nucleosides' anticancer activities, their pharmacokinetic characteristics, and the present state of research into their therapeutic uses. Furthermore, we will investigate the obstacles and possibilities connected with using thio-nucleosides as a novel class of anticancer medications, offering insight on the future prospects and possible effect of this burgeoning field of cancer therapies.

Тионуклеозиды, группа химических веществ, получаемых из нуклеозидов путем замены атома кислорода атомом серы, привлекли большое внимание в исследованиях рака из-за их потенциального противоракового действия. Необычная химическая структура тионуклеозидов наделяет их специфической биологической активностью, что делает их возможными для лечения рака. В этой статье будет рассмотрена роль тионуклеозидов как противораковых препаратов и то, как они ограничивают рост раковых клеток и вызывают апоптоз. Тионуклеозиды продемонстрировали исключительные цитотоксические эффекты на различные линии раковых клеток, что делает их многообещающей мишенью для будущих доклинических и клинических исследований. Их способность вмешиваться в метаболизм нуклеиновых кислот и нарушать механизмы репликации и восстановления ДНК в раковых клетках сделала их жизнеспособными химиотерапевтическими агентами. Кроме того, тионуклеозиды продемонстрировали способность преодолевать лекарственную устойчивость, что является серьезным препятствием в лечении рака, открывая новые пути для создания эффективных противораковых лекарств. В этой статье мы рассмотрим молекулярные процессы, лежащие в основе противораковой активности тионуклеозидов, их фармакокинетические характеристики и современное состояние исследований их терапевтического применения. Кроме того, мы будем исследовать препятствия и возможности, связанные с использованием тионуклеозидов в качестве нового класса противораковых препаратов, предлагая понимание будущих перспектив и возможного эффекта этой растущей области лечения рака.

*Keywords:* Thio-nucleosides, modified nucleosides, cancer cell lines, cell culture.

*Ключевые слова:* Тионуклеозиды, модифицированные нуклеозиды, линии раковых клеток, клеточные культуры.

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