ISSN: 2710-0723

Toxicity Study of Sulfonamides Antibiotics

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Abstract

Antibiotics refer to organic substances produced by plants, animals, microorganisms and other organisms in the course of their life activities or obtained by other methods, which can selectively inhibit or affect other organisms at low concentrations. According to the chemical structure, sulfonamides (SAs), tetracycline, etc. can be divided into sulfonamides, and veterinary antibiotics, agricultural antibiotics, medical antibiotics, etc. can be divided into sulfonamides according to the source. Antibiotics can inhibit cell growth and reproduction, and have been continuously synthesized since the advent of penicillin in 1929. At present, antibiotics have become one of the most widely used and used drugs in the world, not only for the prevention and treatment of human and animal diseases, but also as animal feed.

Keywords

Antibiotics; Sulfa; Antibiotic.

1. Toxicity Test of Sulfonamides

1.1. Luminous Bacteria

In 2010, Jiang et al.used luminescent bacteria to detect the toxicity of antibiotics such as Sas, EC50(36.39~).

938.42 mg·L-1) reflected the difference of toxicity to some extent. In 2012, Zou et al.studied the combined effect of sulfamethoxazole and trimethoprim on luminescent bacteria, and found that the acute combined effect of the two was antagonistic, while the chronic combined effect was synergistic. In 2012, Shi Ying [60] found that EC50 of sodium sulfamethoxine, sodium sulfahexamethoxine and sodium sulfadiazine against Vibrio Q67 in Qinghai were 454.516, 476.835 and 871.196 mg·L-1, respectively. In 2013, Wei Yimeiused Vibrio Fischii as the test organism to determine the inhibitory effects of three antibiotics, trimethoprimidine, sulfamethoxazole and sulfamethoxazole, on Vibrio Fischii at different concentrations, and found that sulfamethoxazole was highly toxic to Vibrio Fischii, and the corresponding EC50 concentration was 16 mg·L-1. In 2013, Cong Yongping et al. found that Sas mainly showed additive and antagonistic effects on binary equal acute combined toxicity of luminous Bacillus. In 2014, An Yiqi et al. [62] measured the combined acute toxic effects of quorum-sensing inhibitors and Sas on Vibrio fyi, and the results showed that the combined effects of furanones, pyrroliones, pyrrole compounds and Sas binary toxicity ratio were synergistic, additive and

ISSN: 2710-0723

antagonistic, respectively. In 2017, Gao Dan et al. [63] found that when Sas combined with quorum sensing inhibitors acted on Vibrio Fesii, the combined toxicity to growth and luminescence was antagonistic and additive, respectively.

1.2. Green Algae

In 2004, Eguchi et al. determined the growth toxicity of a variety of veterinary antibiotics to C. crenalis, among which the EC50 of sulfamethoxazole, sulfadiazine and sulfadimethoxil were 1.5, 2.2 and 2.3 mg·L-1, respectively. In 2008, Yang et al. studied the chronic combined toxicity of 12 kinds of antibiotics on C. notalis and found that Sas showed additive effect. In 2014, Wan Ban et al. studied the toxic effects of erythromycin, ciprofloxacin and sulfamethoxazole on C. aureus and found that erythromycin was more toxic to C. aureus. In 2017, Zhou Xudong studied the effects of Sas and tetracycline antibiotics on microcystis aeruginosa and Microcystis microcystis. The results showed that the 96h EC50 of sulfadiazine and sulfamethoxazole on microcystis microcystis was 10.425 and 3.564 mg·L-1, respectively. The effects of oxytetracycline and sulfamethoxazole on the combined toxicity of microcystis aeruginosa and microcystis were antagonistic and partial addition, respectively. In 2018, Zhang Xiaohan et al. analyzed the sensitivity of green algae to different concentrations of antibiotics, and the results showed that the semi-inhibitory concentrations of sulfame-6-methoxidine and sulfamethoxazole on Chlorophora obliqua were 7.20 and 9.89 μg·mL-1, respectively.

1.3. Animals

In 2006, Hu Yuanyuan found that sulfadiazine had certain reproductive toxicity to mice and toxic effect on sperm. In 2009, Liguoro et al. determined the acute toxicity (48h) of 6 common Sas and their synergists to Daphnia magna, with EC50 ranging from 3.86 to 277 mg·L-1, and the combined toxicity of sulfamethazine and trimethoprimidine to daphnia magna at acute exposure showed a combination effect. In 2013, Wei Yimei measured the effects of three antibiotics, trimethoprimidine, sulfamethoxazole and sulfamethoxazole, on the activities of Daphnia magna at different concentrations, and found that sulfamethoxazine was less toxic to daphnia magna, and the maximum non-effective concentration was higher than 200 mg·L-1. The EC50 for 48h toxicity of sulfamethoxazole to Daphnia magna was 103 mg·L-1, and the combined toxicity of trimethoprim and sulfamethoxazole to daphnia magna was simply additive. In 2015, Xie Meiping et al. conducted three Sas exposure experiments targeting the metabolic capacity of zebrafish, and found that glutathione S-transferase activity and malonaldehyde content under sulfadiazine had significant changes, suggesting that sulfadiazine had potential threats to water environment. In 2018, Liu Lifi et al. found that zebrafish embryos exposed to low concentration of sulfamethoxazole (0.001 mg·L-1) had strong teratogenicity, while high concentration exposed zebrafish embryo mortality increased significantly and hatchability was inhibited.

2. Indicator Organisms for Toxicity Testing

2.1. Chlorophora Obliqua

As the basic link of aquatic food chain, algae is the primary producer in water. Under the action of light, they absorb inorganic salts and carbon dioxide and provide oxygen and food for invertebrates, fish and other organisms. Their production and diversity directly affect the function and composition of aquatic ecosystem. The presence of algae is of great significance to both water productivity and self-purification capacity.

Algae can form a unified whole and interact with the surrounding environment, its growth cycle is short, it is easy to culture, it is sensitive to toxic substances, and the impact of pollutants on algae at the multi-generation and population level can be evaluated in a relatively short time, and it has been regarded as an ideal experimental material since the 1980s. If algae testing is

ISSN: 2710-0723

included in ecosystem testing, the ability of the test system to predict the most sensitive ecosystem can be greatly improved. At home and abroad, algae is used to test the toxicity of chemicals, and a number of algae testing standard methods have been selected and established.

Dictyophylla is a genus of Dictyophyllidae in the order Chlorella, chlorophyta, and usually consists of 4 to 8 cells or 16 to 32 cells, rarely single cells. Most are oval or spindle shaped, arranged in 1 to 2 or more columns with long axes. Gridiella is a common planktonic algae in fresh water, which often thrives in nutrient-rich standing water and is highly adaptable.

Among all aquatic organisms, algae is the most sensitive to the toxic effects of Sas. Studies have shown that almost all Sas can produce toxic effects on algae. Biaik et al. selected 12 different Sas to study the alga haida and found that Haida is very sensitive to Sas. EC50(24h) ranges from 1.54 to 32.25 mg·L-1. The three Sas most toxic to green algae are sulfamethoxazole, sulfadiazine and sulfamethoxypyridazine.

2.2. Vibrio Qinghaiensis Q67

Luminescent bacteria are a class of gram-negative facultative anaerobic bacteria, which can emit fluorescence at 450-490 nm wavelength, and their luminescence intensity is certain under certain environmental conditions. The fluorescence is closely related to their own metabolism, and the intensity of fluorescence reflects their own metabolism. When luminous bacteria are exposed to external pollutants (pesticides, heavy metals, antibiotics, etc.), their luciferase will be inhibited, and the fluorescence intensity will be reduced. A luminescence detector was used to detect the decrease in luminescence intensity when exposed to pollutants compared with the control group, and the toxicity of pollutants to luminescent bacteria could be obtained.

The application of luminescent bacteria toxicity test technology to the detection of environmental toxicants originated from the 1980s of the last century, because of its fast detection speed, high sensitivity, simple equipment, and excellent scalability, it has been rapidly developed in the toxicity detection of environmental samples. Studies have shown that the toxicity of most organic pollutants to luminous bacteria is positively correlated with the toxicity to various aquatic organisms, and this method was listed as the standard method for environmental biological toxicity detection in China in 1995 (GB/T16441-1995).

Light-emitting bacteria can be divided into Marine light-emitting bacteria and freshwater light-emitting bacteria, etc. Most light-emitting bacteria belong to Marine light-emitting bacteria, while very few belong to freshwater light-emitting bacteria. Currently, among freshwater light-emitting bacteria, only Vibrio Qinghaiensis is non-pathogenic, so it has attracted wide attention. Vibrio Qinghaiensis is a kind of freshwater luminescent bacteria isolated by Professor Zhu Wenjie from the body surface of Gymnasia Cypris in Qinghai Lake. His research group has successfully developed a fast and sensitive comprehensive toxicity detector for environmental pollutants, and has formed a complete system, which has been widely used in the monitoring of environmental pollutants, and obtained a high evaluation.

Ding Tingting et al. studied the concentration ratio dependent antagonism of SAs against Vibrio Q67 in Qinghai province. The toxicity sequence of five antibiotics to Q67 was as follows: sulfamethoxazole > sulfachlorpyridazine > Sulfapyridine > Sulfadiazine > sulfadiazine; According to CA model, 7 mixed systems showed additive effect and 3 mixed systems showed antagonistic effect. Chen Qiong [88] studied the toxicity of five kinds of SAs, including sulfachlorpyridine (SCP), sulfadipyrimidine (SM2), and sulfapyridine (SPY), to Vibrio Q67 in Qinghai Province, and the results showed that the SCP-SPY mixed system basically showed a law of antagonism in medium and low concentrations. The SCP-SM2 mixed system basically shows a law of adding effect in medium and high concentrations.

ISSN: 2710-0723

3. Research Status at Home and Abroad

There are abundant reports on the toxicity of SAs. According to the conditions "subject =(sulfonamide antibiotics or sulfonamides)" AND "subject =(toxicity)", the data from 2000 to 2019 were retrieved (the retrieval time is September 2019), and 3944 relevant literatures were retrieved. The total cited frequency is 141112, the total cited frequency without self-cited is 134562, and the average number of citations for each item is 35.78. The number of published articles in each year in the past 20 years is shown in Figure 1.1. It can be seen that the research achievements in the field of toxicity research of SAs have shown an increasing trend in recent years.

Acknowledgments

This work was supported by the Scientific Research Item of Shaanxi Provincial Land Engineering Construction Group (2021WHZ0092) .

References

[1] QIAN-QIAN Z, GUANG-GUO Y, CHANG-GUI P, et al. Comprehensive evaluation of antibiotics emission and fate in the river basins of china: source analysis, multimedia modeling, and linkage to bacterial resistance[J]. Environmental Science & Technology, 2015, 49(11): 6772-6782.

[2] Zhu W, Liu J,Yu S.et al.Ag loaded WO3 nanoplates.for.efficient photocatalytic degradation of sulfanilamide and their bactericidal effect.under visible light irradiation[J].Journal of Hazardous Materials.2016,318:407-416.

[3] BAI Y, RUAN X, WANG F, et al. Sulfonamides removal under different redox conditions and microbial response to sulfonamides stress during riverbank filtration: A laboratory column study [J]. Chemosphere, 2019, 220:668-677.

[4] BARAN W, ADAMEK E, ZIEMIAŃSKA J, et al. Effects of the presence of sulfonamides in the environment and their influence on human health[J]. Journal of Hazardous Materials, 2011, 196(1): 1-15.