Journal of Advanced Research in BioChemistry and Pharmacology
Volume 1, Issue 1&2 - 2018, Pg. No. 46-47
Peer Reviewed & Open Access Journal

Research Article

Uses of Diazo Dyes as Drugs

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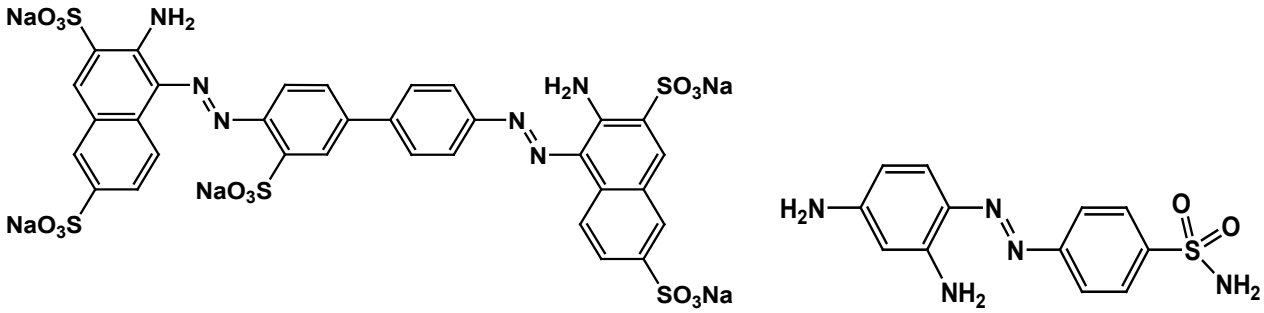
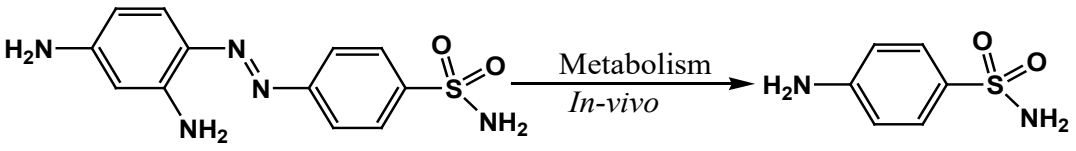
Dyes were used for dying textiles and other materials and in biology, these were used for identifying various types of pathogens like bacteria, protozoa, etc. Paul Ehrlich was working on biological properties of these dyes on blood cells, demonstrating the specific staining of parts of certain leucocytes, the basis of hematology. In order to test the hypothesis that it is possible to stain pathogens specifically and perhaps be killed without harming the host, Ehrlich's laboratory focused first on malaria protozoa using methylene blue and related dyes. For five years, Ehrlich and his associates studied hundreds of synthesized dyes leading to the first synthetic antimalarial, Tryphan red in 1904.[1] However, Tryphan red did not have anti-malarial potency needed for an effective human cure. Ehrlich thought that an introduction of heavy metal atoms such as arsenic might improve its potency and he introduced arsenic into the dye and discovered Atoxyl, which was successful in treatment of malaria. However, since it contained arsenic, its long-term use led to hepatotoxic effects and hence its use was discontinued. He then shifted his research interest towards finding a drug for syphilis. He modified the structure of Atoxyl and produced two important molecules namely Salvarsan and Neosalvarsan in 1912, which were less toxic and highly effective against syphilis. This stimulated researchers to look towards dyes as possible drug candidates. The systematic synthesis of Mietzsch and Klarer azo dyes for their antimicrobial activity, Sulphonamide azo dyes were included for the study as they were relatively easy to synthesize and had improved staining properties. In 1932, study of bright red dye later to be named as Prontosil found that it caused remarkable cures of *Streptococcal* infections of mice. However, Prontosil was inactive on bacterial cultures.[2] For his work, Gerhard Domagk was awarded the Nobel Prize.



Tryphan red Prontosil

Prontosil's inactivity *in vitro* but excellent activity *in vivo* attracted much attention. In 1935, through series of SAR studies, the azo linkage of Prontosil was metabolically broken to release the active ingredient, sulphanilamide.[3] Following Prontosil's dramatic successes, cascade of sulphanilamide derivatives were synthesized and tested over 4500 by 1948 alone. From these, only about a dozen were approved for clinical use. With the discovery of Penicillin in 1940s and emergence of side effects of sulphanilamides, the use of diazo compounds as possible drug candidates and sulphanilamides for clinical purpose was declined. However, even after more than 60 years of discovery, some of the sulphanilamides like sulphadiazine, sulphamethaoxazole and sulphadimidine are still clinically used for some disorders.



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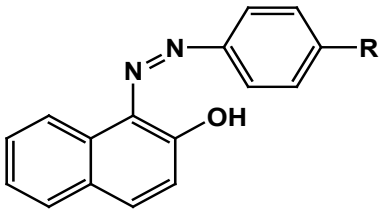
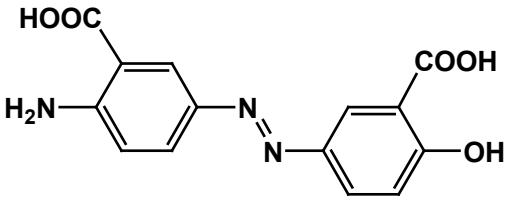
How to cite this article: Asif M, Uses of Diazo Dyes as Drugs. *J Adv Res BioChem Pharma* 2018; 1(1&2): 46-47.

Prontosil Sulphanilamide

Research on toxicity studies of diazo compounds indicated that due to *in vivo* transformation into amine group which binds to CYP enzyme, diazo compounds produce toxicity. However, with the emergence of antibiotic-resistant bacterial strains and newer diseases, fresh attempts were made to use diazo functionality for discovery of lead molecules. This has resulted in publication of many research papers where considerable work has been done on the synthesis and biological and pharmacological evaluation of novel compounds containing azo group.

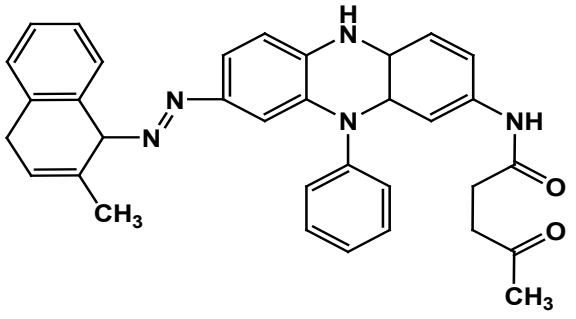
Diazo compounds containing naphthalene moiety and tested their biological activity against various pathogens and found that some of the azo compounds exhibited significant activity.[4] Ulcerous colitis is a serious chronic intestinal disease localized to large intestine. Several novel azo dyes **2** are prepared and evaluated for their usefulness in treatment of ulcerous colitis.[5]





1 R=SO_2NH_2, substituted amino **2**

Molecules which contain diazo group were tested for PARP-inhibiting activity. Some of the compounds **3** and **4** were found to exhibit prominent PARP-inhibiting activity. Poly(ADP-ribose)polymerase is a type of enzyme located in nuclei of cells of various organs including muscle, heart and brain cells.



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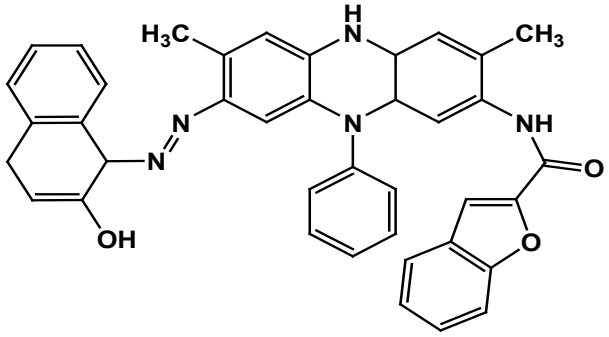

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PARP inhibitors play a vital role in treatment of various ailments such as neuro-degenerative diseases, stroke, Alzheimer's disease, Parkinson's disease, Huntigton's disease, chronic pain, ischemia hypoxia, and trauma.[6]

Conflict of Interest: None

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Date of Submission: 2018-01-22
Date of Acceptance: 2018-02-22