



The Azo Derivatives of Salicylic Acid

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ABSTRACT

Azo dyes are extremely important in variety of industries for variety of technical purposes. The compounds containing azo grouping are most widely used as synthetic colorants. Azo dyes are generally synthesized starting from primary aromatic amines by diazotization and coupling with e.g. phenols or primary aromatic amines or their carboxylic derivatives such as salicylic acid etc. The chemical structures of synthesized compounds were studied for confirmation of structure using varied type of analytical data and the spectroscopic techniques like UV-Visible, FTIR, Mass spectra, ^1H - and ^{13}C -NMR. These compounds have numerous applications such as antioxidants, as pigments, the polymeric biodegradable prodrugs and many pharmacological uses.

Keywords: Azo dyes; salicylic acid derivatives, coupling reaction; diazotization.

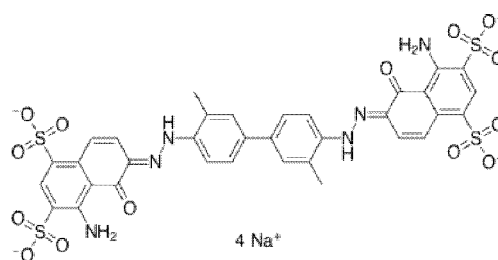
INTRODUCTION

Azo compounds or dyes are characterized by the presence of the azo moiety ($-\text{N}=\text{N}-$) in their structure, conjugated with two, distinct or identical, mono- or polycyclic aromatic or heteroaromatic systems. Because of their specific physico-chemical properties and biological activities, they have found a broad application viz in pharmaceutical, cosmetic, food, dyeing or textile industry and analytical chemistry. However, the most typical and popular field of utility remains as their coloring function. Azo dyes are the largest and the most versatile class of dyes.

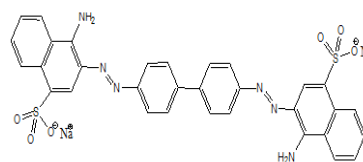
The azo compounds are applicable for biocidal treatment of textile materials because they exhibit biological activity¹. Azo compounds are well known for their medicinal importance and are recognized for their applications as antidiabetics², antiseptics³, antineoplastics⁴, antibacterial⁵⁻⁶ and antitumor⁷. They are involved in a many biological reactions such as inhibition of DNA, RNA, carcinogenesis, protein synthesis and nitrogen fixation^{8,9}. Azo compounds are valuable in the medicinal and pharmaceutical fields¹⁰ and probably the azoimine linkage might be responsible for the biological activities displayed by some Schiff bases as reported¹¹⁻¹².

The azo compounds viz. Evans blue, **1** and Congo Red, **2** are being studied as HIV inhibitors of viral replications¹³. The existence of azo moiety show antibacterial and pesticidal activities. Recently, azo group containing compounds as antimicrobial agents has been the subject of study reported by H. N. Chopde¹¹, A. H. Shridhari¹⁴ and C. J. Patil¹⁵⁻¹⁷. Synthesis of most azo compounds involves diazotization of a primary aromatic amine, followed by coupling with one or more nucleophiles. Thus, benzoic, phenolic, salicylic and naphtholic compounds undergoes diazotization reactions. Because of variety applications, azo compounds, it is interesting to study synthesis of such salicylic azo compounds and their derivatives in order to

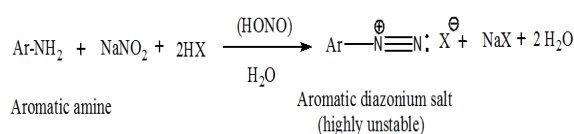
explore the newer potentials of such compounds. Few times azo compound is often described as a chromogen in the literature¹⁸. The amino- and hydroxy-groups are commonly used coupling components¹⁹. The emergence of diverse classes of synthetic dyes including azo dyes occurred due to constant effort to find specific dye for application in diverse materials of industrial importance which include, but not limited to textile fabric²⁰, ink-jet printer, paper, leather, aluminium sheet²¹. Furthermore, azo compounds also have a many applications in photo-industry such as photodynamic therapy, photographic or electro-photographic systems and are dominant organic photoconductives^{7,14}.



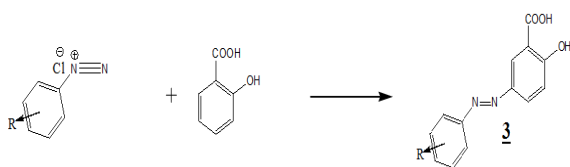
1 Evans Blue



2 Congo Red



Scheme-1: General Reaction Mechanism of Diazonium Salt formation.



Scheme-2: Coupling Reaction with Salicylic acid.

Literature Survey and Discussion:

In the last century, azo compounds constitute one of the largest classes of industrially synthesized (including natural pigments) organic compounds, potent in drug and the cosmetics²²⁻²³. Segmented polyurethanes containing azo aromatic groups in the main chain were synthesized by reaction of 3,3'-azobis(6-hydroxybenzoic acid) (ABHB), 5-[4-(hydroxyphenyl)azo] salicylic acid (HPAS), and 5-[1-hydroxynaphthyl]azo] salicylic acid (HNAS) with hexamethylenediisocyanate (HDI). All the studied azo polymers showed good thermal stability with decomposition temperature above 195 °C²⁴. The p-aminobenzoic acid and its salicylic acid derivatives (PAS) are bacteriostatic and decrease the respiration of tubercle bacillus (antitubercular drugs). PAS is preferred to the other benzoates or salicylates as it is less toxic and it prevents rapid development of resistant strains. It is more effective when it is given in combination with streptomycin fever during the administration of salicylate signals for the discontinuation of the drug immediately²⁵.

The azo dyes based on salicylic acid-formaldehyde polymer as a polymeric ligands were used to form metal chelates with Cu⁺², Zn⁺², Co⁺², Fe³⁺, UO₂²⁺, Mn⁺² and Ni⁺². The ion-exchange and antibacterial and antifungal properties of these polymers were also studied. The colours of azo dyes include different shades of yellow, red, orange, brown, and blue and hence used as an indicator compounds²⁶.

Few azo compounds are pharmaceutically acceptable salts and process for preparing the 2-[(p-(2-pyridylsulfamoyl)phenyl)azo]hydroxybenzene; 3-[(p-(2-pyridylsulfamoyl)phenyl)azo] salicylic acid; and 5-[(p-(4-(2-pyridylanilino))-N phenyl)azo]salicylic acid²⁷.

Azo compound represents the largest class of dyes, their breakdown products are toxic and or mutagenic to life. They are studied for evaluation of their resistance against the growth of fungi organisms, antihelminthic properties and dyeing abilities on cotton fabrics, biodegradation of different azo compounds and anaerobic property²⁸. Azo-Bis salicylic acid and its salt which are useful on the treatment of inflammatory conditions of the intestine²⁹. From methyl salicylate and 2-amino-2-(hydroxymethyl)propane-1,3-diol, or 2-amino-2-methylpropane-1-ol, the 2-oxazoline derivatives as well as mono and bis-derivatives of salicylic acid and biological activity were reported. Reactions using microwave irradiation in the presence of PTC (tetrabutylammonium bromide) or metallic sodium as catalyst, as well as by conventional heating were reported. Some of the mono-

and bis-salicyloyl derivatives were transformed to the corresponding phenyl-azo derivatives. The antioxidant and cytotoxic activities of the synthesized derivatives were evaluated in a series of *in vitro* tests. Compounds inhibited growth of MDA-MB-231 cells at a nanomolar concentration showed high cytotoxicity against MCF7 cells, whereas compounds showed high activity against K562 cells³⁰.

Iron complexes of reactive azo dyes were studied by R. Hrdina³¹. A set of reactive mordant azo dye compound was prepared by diazotization of aromatic amines and their subsequent coupling reaction with secondary components. Dyed wool samples were treated (mordanted) with iron salts Fe(II), Fe(III) and a chromium salt (CrF₃). The iron mordant dyeing showed acceptable wash fastness and light fastness comparable with chromium complexed dyes³¹, reactive dyes, iron mordant dyes, wool, wash fastness, light fastness.

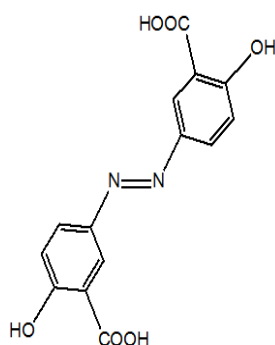
B. K. Patel³² have synthesized five sulfanilamide derivatives. Then all sulfanilamide derivatives diazotization with NaNO₂ and HCl at 0-5°C. Then the azo dye was synthesized by the coupling of diazonium salt of sulfanilamide derivatives with salicylic acid ligand. After the synthesis, compounds were characterized by chemical as well as instrumental methods, like melting point, elemental analysis, UV-visible spectroscopy and IR spectral studies.

Ewelina³³ has proposed that azo dyes – a fatal threat or a new generation of drugs? In 1858 Griss developed the azo coupling reaction and obtained first azo dye–Aniline Yellow. Nowadays, around 10,000 of these compounds are described and more than 2000 are applied to color various materials. Azo dyes are characterized by the presence of the azo moiety (–N=N–) in their structure, conjugated with two, distinct or identical, mono- or polycyclic aromatic systems. Because of their specific physico-chemical properties and biological activities, they have found a broad application in pharmaceutical, cosmetic, food, dyeing or textile industry and analytical chemistry. However, the most typical and popular field of utility remains their coloring function. Azo dyes are the largest and the most versatile class of dyes. They possess intense bright colors, in particular oranges, reds and yellows. In addition, azo dyes exhibit a variety of interesting biological activities. Medical importance of these compounds is well known for their antibiotic, antifungal and anti-HIV properties. On the other hand they bring a certain danger for health and environment because of cancer- and mutagenicity. In this review, selected synthetic strategies and biological activities of azo dyes are presented, the latter in the context of a therapeutic potential and a hazard connected with their production and application.

H. H. M. Abdull-Allah³⁴ have synthesized from salicylic acid and phenyldiazoniumchloride salt, 3-N-(4'-Hydroxy-3'-substituted phenyl)carbamoyl-1-methylpyridinium iodide

derivatives and 3-carbamoyl-1-(N-(4'-hydroxy-3'-substituted phenyl)carbamoyl) methyl pyridinium chlorides were synthesised and tested some of them for their analgesic and anti-inflammatory activities by hot plate test and carageenin-induced hind paw edema model, respectively. 3-N-(4'-hydroxy-3'-substituted phenyl)carbamoyl-1-ethylpyridinium iodides revealed the most potent analgesic and anti-inflammatory activities in comparison to sulfasalazine and 5-ASA. In addition, ulcerogenicity, LD 50, in-vivo and in vitro cleavage and pH stability of 3-N-(4'-hydroxy-3'-substituted phenyl)carbamoyl-1-methylpyridinium iodides were also determined.

Lamber and Pitzele³⁵ have mentioned in the present invention relates to novel compounds and a method for the prophylaxis and treatment of Inflammatory Bowel Disease (IBD) via the administration of an effective amount in a suitable pharmaceutical dosage form of an azobenzene compound **4** or a pharmacologically acceptable salt, which is reductively cleaved to 5-aminosalicylic acid (5-ASA) by bacteria in the large intestine.

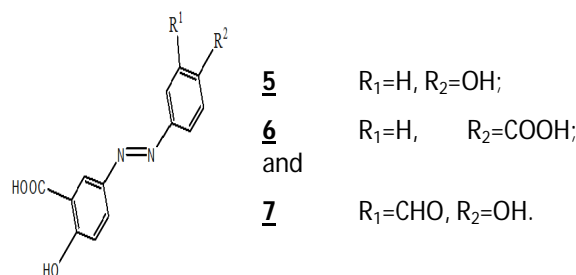


Popa³⁶ have studied three dyes, as concentration in the paint grows, the luminosity gets fainter and thrown light on the coloring power of this class of compounds by studying the colour properties of some azoic dyes derivatives of salicylic acid. The one containing nitrogen at the coupling component provides a higher luminosity than the dyes, which also contain sulphur. From the two dyes containing sulphur, the one with a supplemental benzene nucleus is less luminous. This behaviour is due to strengthen of aromatic conjugation, which causes a bathochroma displacement, thus a darkness in colour as an outcome of decreasing luminosity. The dye containing only nitrogen at the coupling component tends to provide in visual perception more red, in direct ratio to concentration. The dye with a stronger conjugation of the coupling component tends to provide less red at high concentrations, which means a shifting towards green in the colour space. The dye containing a coupling component with nitrogen provides more yellow compared to sulphur containing dyes. The samples are different regarding their dye concentration. The hue, luminosity and saturation are studied as well as their colouring power. The colouring power of all three dyes is strong, which makes them very efficient in industrial use.

Bernt Jabes Lindberg³⁷ have studied amine addition salts of 5-[p'-(2-pyridylsulfamyl)-phenyl azo J-salicylic acid are provided. The amine-is represented, by the formula: **A-R** wherein **A** is either -NR₁R₂ or 4-morpholino, or piperidino; and wherein **R** is either tris-hydroxymethyl-methyl, 2-hydroxy ethyl, 2-hydroxypropyl, 3-hydroxypropyl, 2-methoxyethyl, 3,4,5,6-tetrahydroxyhexanal-2-yl, and 2,3,4,5,6-pentahydroxyhexyl; and R₁ and R₂ (pl see **Table-1** for values) are either hydrogemmethyl, ethyl, or 2-hydroxyethyl. The present compounds can be used for the treatment of ulcerative colitis and rheumatoid.

Reddy³⁸ have stated two simple, sensitive, accurate and economic methods have been developed for the quantitative estimation of mesalamine and its formulations. **Method-A** is based on the diazotization of primary amine group of mesalamine with sodium nitrate and hydrochloric acid followed by coupling with resorcinol to form a orange colored chromogen with a characteristic absorption maximum at 460 nm. **Method-B** is based on the reaction of the mesalamine with vanillin in acidic medium producing Schiff s base having absorption maximum at 395 nm. The methods were successfully applied to the determination of mesalamine in pharmaceutical formulations.

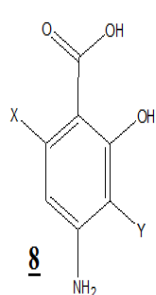
Henry Mirocourt³⁹ has used azo dyes and ortho-oxy-azo dyestuffs for synthesis of complexes of chromium. Garjani⁴⁰ have synthesized Three azo prodrugs; 4,4 - dihydroxy-azobenzene-3-carboxylic acid **5**, 4-hydroxy-azobenzene-3,4-dicarboxylic acid **6**, 4,4-dihydroxy-3-formyl-azobenzene-3-carboxylic acid **7**, and their polyethylene glycol (PEG 6000) derivatives were synthesized and demonstrated the effect and relation of protective and anti-inflammatory effects of azo and azo-linked polymeric prodrugs of 5-aminosalicylic acid (5-ASA) on acetic acid induced colitis in rats are investigated. Results of their investigation provide experimental evidence supporting new cytoprotective, anti-inflammatory and anti-edema properties of the azo derivatives of 5-ASA and their PEGylated prodrugs.



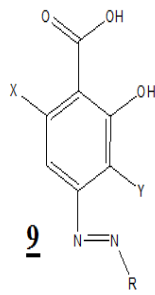
For decades, sulphasalazine, an azo-compound derived from sulphapyridine and 5-aminosalicylic acid (5-ASA), has been the only valuable non-cortico-steroid drug in the treatment of inflammatory bowel disease⁴¹. Literature⁴² showed that the pharmacologically active moiety in sulphasalazine for the treatment of these diseases was 5-

ASA. Moreover, it has been shown that the metabolite sulphapyridine was largely responsible for the side-effects of sulphasalazine⁴¹. Consequently, this resulted in a number of new 5-ASA formulations (mesalazine, olsalazine, balsalazine) for topical and oral use. 5-ASA is partially resorbed, particularly in the acetylated form and eliminated as such in the urine. The colon is the predilected place for this acetylation since in the small bowel there is a lack of the responsible bacterial flora. Hence, 5-ASA is readily absorbed as such in the small bowel. How far this may form a rationale for a possible difference in nephrotoxicity for the different preparations remains scope for research.

Herbert Kracker⁴², have reported study of the 4-Amino-2-hydroxybenzene-1-carboxylic acid, where X and Y may be equivalent to H or other substituent. These, **8** type of compounds are used to synthesized valuable azo-dye stuffs. The compounds of the type **8** can be coupled with varied phenolic compounds (like salicylic acid, naphthol sulphonic acids and amino naphthol sulphonic acids etc.) and converted to compounds of type **9**, are used as azo-dye stuffs as well.



8
4-Amino-2-hydroxybenzene-1-carboxylic acid



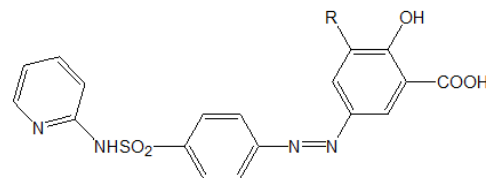
9
Substituted-4-azo-(3,6-disubstituted-2-hydroxybenzene)-1-carboxylic acid

Such compounds improve the fastness property of the dye-stuff or can be applied to fiber directly depending upon the group attached to the molecule. In the present patent there are primary mistakes in nomenclature of the compounds in the Table they have given therein. So it is not correct, that criticize the same.

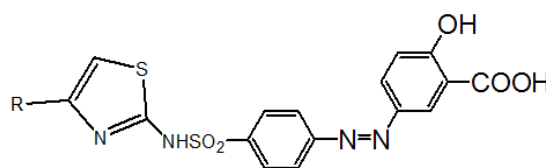
J. A. Jalani⁴³, the syntheses of 4-aminophenylbenzoxazol-2-yl-5-acetic acid, (an analogue of a known nonsteroidal anti-inflammatory drug [NSAID]) and 5-[4-(benzoxazol-2-yl-5-acetic acid)phenylazo]-2-hydroxybenzoic acid (a novel mutual azo prodrug of 5-aminosalicylic acid [5-ASA]) are reported. The structures of the synthesized compounds were confirmed using infrared (IR), hydrogen-1 nuclear magnetic resonance (¹H NMR), and mass spectrometry (MS) spectroscopy. Incubation of the azo compound with rat cecal contents demonstrated the susceptibility of the prepared azo prodrug to bacterial azoreductase enzyme. The azo compound and the 4-aminophenylbenzoxazol-2-yl-5-acetic acid were evaluated for inflammatory bowel diseases, in trinitrobenzenesulfonic acid (TNB)-induced colitis in rats. The synthesized diazo compound and the 4-aminophenylbenzoxazol-2-yl-5-acetic acid were found to be as effective as 5-aminosalicylic acid for ulcerative

colitis. The results of this work suggest that the 4-aminophenylbenzoxazol-2-yl-5-acetic acid may represent a new lead for treatment of ulcerative colitis.

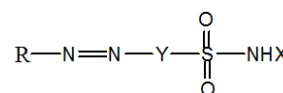
Eric Emil⁴⁴ have reported following heterocyclic sulphonamido azo compounds **10**(a, b, c) and . The molecule **10**a and **11**a forms water soluble salt with alkali.



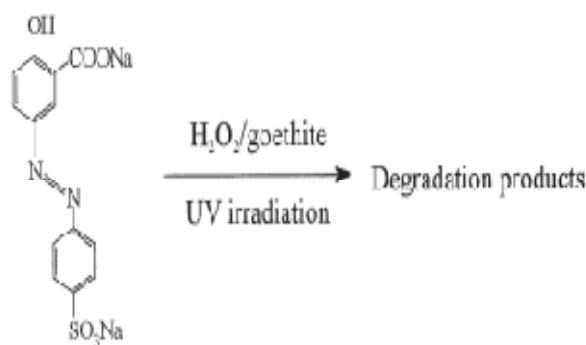
10 a) R = -H; b) R = -CH₃ c) -COOH



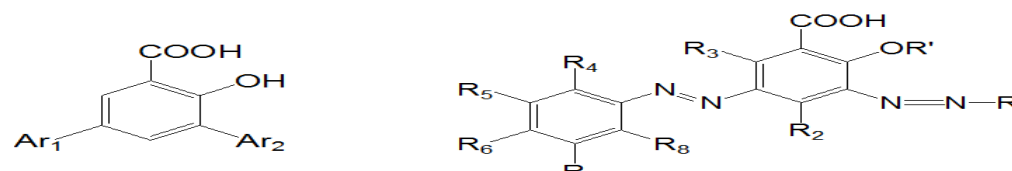
11a) R = -H and b) R = -CH₃.



The photodegradation of Mordant Yellow 10 (MY10), a kind of azo dye, in aqueous dispersions of H₂O₂/hematite (alpha-Fe₂O₃), goethite (alpha-FeOOH) and akaganeite (beta-FeOOH) at neutral pHs under UV-light irradiation was examined. The fastest degradation rate of MY10 was obtained with goethite, the reports made by Ju He⁴⁵.



The formation of OH in the photoreaction process was detected by ESR spin-trapping technique. A possible mechanism of heterogeneous photo-Fenton reaction was proposed by Ju He⁴⁵.

Table 1: The Skeleton, Substituent's position and Applications of the azo moiety containing compounds from Salicylic acid.

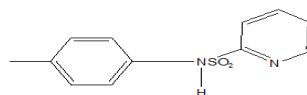
No.	R'	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈	Ref	Application	R''	R'''
Ar-N=N-Ar-N=N-Ar													
1	H	H	H	H	H	H	-OH	H	H	24	As polymeric biodegradable prodrug	-	-
2	H	H	H	H	H	COOH	-OH	H	H				
3	H	H	H	H	H	H	-OH	-C ₄ H ₄ -					
4	link-	H	H	H	H	-COOH	-O-C=O-NH-link	H					
5	link-	H	H	H	H	H		H					
6	link-	H	H	H	H	H	-SO ₃ H	-C ₄ H ₄ -					
7	-	H	H	H	H	H		H					
8	-	H	H	H	H	H	H	H	-SO ₃ H	25	The colours of azo dyes include different shades of yellow, red, orange, brown, and blue used for textile		
9	-	H	H	H	H	H	NO ₂	H	H				
10	-	-CH ₂ -5-CH ₂ -5-Sali	H	H	H	H	H	H	H				
11	-	-CH ₂ -5-Sali-5-Sali	H	H	H	H	H	H	H	26	Studied for the chelation ion-exchanging properties of the polymers	-	-
12 ψ	-	H	H	H	H	H	-NH-SO ₂ -2-Py	H	H				
13*	-	-N=	H	H	-	-	-	-	-	27	Pharmaceutically acceptable and readily soluble salts	-	-
14	-	H	H	H	H	H	-NH-(-Ph-4)-2-Py	H	H				
15	-	H	H	H	H	H	-NH ₂	H	H	28	Antifungal, antihelmentic activities and their dyeing ability	-	-
16	-	H	H	H	H	-NO ₂	-NH ₂	H	H				
17	-	H	H	H	CH ₃	H	-OH	H	H				
18	-	H	H	H	-CH ₃	H	-NH ₂	H	H				
19	-	H	H	H	H	H	-OH	H	H				
20	-	H	H	H	H	-NO ₂	-OH	H	H				
21	-	H	H	H	H	-OSO ₂ R ₂	-CO-O-R ₁	H	H	29	Inflammatory bowel diseases (IBD)	-	H
22	-	H	H	H	H	-OSO ₂ R ₂	-CO-OR ₁	H	H			-	Me
23	-	H	H	H	H	-OSO ₂ R ₂	-CO-OR ₁	H	H			-	Et
24	-	H	H	H	H	-OSO ₂ R ₂	-CO-OR ₁	H	H			-	Pr
25	-	H	H	H	H	-OSO ₂ R ₂	-CO-OR ₁	H	H			-	But

26	-	H	H	H	H	-OSO ₂ R ₂	-CO-OR ₁	H	H			-	Pent
27	-	H	H	H	H	H	H	H	H	30	Studied for antioxidant activities	-NH-CH ₂ -CH ₂ -OH	-
28	-	H	H	H	H	H	H	H	H			-NH-(CH ₂) ₂ -Link	-
29	-	H	H	H	-OH	H	-OH	-N=N-C ₄ H ₄ -RG ₁	H			31	Useful for wool dyeing
30	-	H	H	H	H	H	-NH-SO ₂ -Link	H	H	-	-		
31	H	-	-	-	H	H	-SO ₂ -N-Et ₂	H	H	32	The antioxidant, Antiproliferative and cytotoxic activities of the synthesized derivatives were evaluated in a series of <i>in vitro</i> tests.		
32	H	-	-	-	H	H	-SO ₂ -N-Ph ₂	H	H			-	-
33	H	-	-	-	H	H	-SO ₂ -N-(Ph)Et	H	H			-	-
34	H	-	-	-	H	H	-SO ₂ -N-H(2,4-Cl ₂ -Ph-)	H	H			-	-
35	H	-	-	-	H	H	-SO ₂ -N-H(2,6-Cl ₂ -4-NO ₂ -Ph-)	H	H			-	-
36	-	H	H	H	H	-O-PEG	H	H	H	33	Anti-inflammatory and cytoprotective potency	-	-
37	-	H	H	H	H	H	H	H	H	34	Inflammatory bowel diseases (IBD) with minor side effects	-OH	-
38	-	H	H	H	H	H	H	H	H			-OMe	-
39	-	H	H	H	H	H	H	H	H			-OEt	-
40	-	H	H	H	H	H	H	H	H			-OPro	-
41	-	H	H	H	H	H	H	H	H			-NH ₂	-
42	-	H	H	H	H	H	H	H	H			-NHCH ₃	-
43	-	H	H	H	H	H	H	H	H			-NHet	-
44	-	H	H	H	H	H	H	H	H			-N (Me) ₂	-
45	-	H	H	H	H	H	H	H	H			Piperidino	-
46	-	H	H	H	H	H	H	H	H			Morphonilino	-
47	-	H	H	H	H	H	-OH	-COOH	H	35	In the treatment of (Inflammatory Bowl Disease) IBD	-	-
48	-	H	H	H	H	H	-SO ₂ -NH-Py	H	H			-	-
49	-	H	H	H	H	H	-NO ₂	H	H			-	-
50	-	H	H	H	H	H	-NO ₂	H	H	36	Colour dye	-NH-1,2,4triazole	-
51	-	H	H	H	H	H	-SO ₂ -NH-Py	H	H			-NH-2sub-thiazole	-
52	-	H	H	H	-OH	H	-OH	H	H	37	In the treatment of ulcerative colitis and rheumatoid arthritis	-	-
53	-	H	H	H	H	H	-OH	H	H	38	Determination of mesalamine in pharmaceutical formulation	-	-
54	-	H	H	H	H	H	-SO ₃ H	-C ₄ H ₄ -				-	-
55												39	The products are applicable in industry for dyeing of animal textile fibres.
										40	Azo derivatives of 5-aminosalicylic acid and their pegylated prodrugs	-	-



56	H	-	-	-	H	H	-SO ₂ -NH-Py	H	H	41	For the treatment of patients with chronic inflammatory bowel disease	-	-
57	As describe and disscued in the text									42	Used for synthesizing varied azo dyestuffs -	-	-
58	-	H	H	H	H	H	COOH	OH	H	43	It is for the water soluble azo dyestuff and for the navy-blue shades of good fastness properties.	-	-
Het-Ar-N=N-Ar-N=N-Ar													
59	-	H	H	H	H	H	-SO ₂ -NH-Py	H	H	44	The colored powders with in general slight solubility in water and other usual solvents. In alkaline solution they will generally form more readily soluble salts having a stronger color	-	-
60	-	H	H	H	H	H	-SO ₂ -NH-Thizol-2-yl-	H	H				
61	-	H	H	H	H	H	-SO ₂ -NH-4-Me-Thizol-2-yl-	H	H				
62	-	 Het-2-			H	H	-SO ₂ -NH-Py	H	H				
63	-	- Me	H	H	H	H	-SO ₂ -NH-Py	H	H				
64	-	-COOH	H	H	H	H	-SO ₂ -NH-Py	H	H				
65	H	H	H	H	H	H	SO ₃ Na	H	H	45	photodegradation of Mordant Yellow	-	-

* for entry No. 13 R



Gen. Abbrivations: Cl = Chloro-; Ph = Phenyl-; PEG = Propyl Ethylglycol ; Py = Pyridine; Pyl = Pyrrole; and

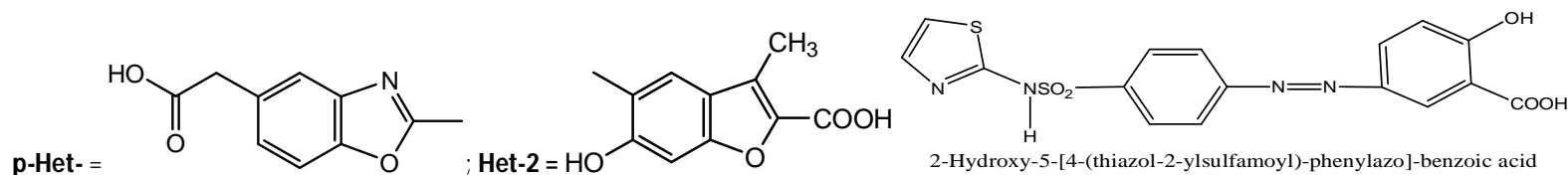


Table 2: The Skeleton, Substituent's position and Applications of the diazo moiety containing compounds from Salicylic acid.

Sr. No.	R	R1-	Ref	Application
1	Naphthyl-	1-Hydroxy naphthyl-4-sulfonicacid	42	Used for synthesizing varied azo dyestuffs.
2	2-Methy-5-methoxyphenyl-	2-Hydroxy naphthyl-3,6-disulfonicacid		



CONCLUSION

The compounds synthesized from the azo derivatives of salicylic acid are useful for many applications such as colours of azo dyes include different shades of yellow, red, orange, brown, and blue used for textile, for wool dyeing and in industry for dyeing of animal textile fibres, for the chelation ion-exchanging properties of the polymers. Pharmaceutically acceptable and readily soluble salts, polymeric biodegradable prodrug, antifungal, antihelminthic activities and their dyeing ability, Inflammatory bowel diseases (IBD), for antioxidant activities. In alkaline solution they will generally form more readily soluble salts having a stronger color. Azo derivatives of 5-aminosalicylic acid and their pegylated prodrugs.

REFERENCES

1. Simu GM, Dragomirescu A, Grad ME, Savoibalint G, Andoni M, Bals G, Azo compounds with antimicrobial activity, 14th Int. Electron. Conf. Syn. Org. Chem. ECSOC-14, 2010, 1–30, (<http://sciforum.net/conference/ecsoc-14/natprod>, accessed on 10-01-2015).
2. Garg HG, Prakash C, Preparation of 4-aryloxy-3,5-disubstituted-(2H)-1,2,6-thiadiazine 1,1-dioxides, *J. Med. Chem.*, 15(4), 1972, 435-436, DOI: 10.1021/jm00273a034.
3. Browning CH, Cohen JB, Ellingworth S, Gulbransen R, The antiseptic properties of the amino derivatives of styryl and anil quinoline, *Journal Storage*, 100, 1926, 293-325.
4. Child RG, Wilkinson RG, Tomcu-Fucik A, Effect of substrate orientation of the adhesion of polymer joints, *Chem. Abstr.*, 87, 1977, 6031.
5. Khalid A, Arshad M, Crowley DE, Accelerated decolorization of structurally different azo dyes by newly isolated bacterial strains, *Appl. Microbiol. Biotech.*, 78, 2008, 361-369, DOI: 10.1007/s00253-007-1302-4.
6. Pagga U, Brown D, The degradation of dyestuffs in aerobic biodegradation tests, *Chemosphere*, 15, 1986, 479-491, DOI: 10.1016/0045-6535(86)90542-4.
7. Thoraya A, Farghaly, Abdallah ZA, Synthesis, azo-hydrazone tautomerism and antitumor screening of N-(3-ethoxycarbonyl-4,5,6,7-tetrahydro-benzo[b]thien-2-yl)-2-arylhydrazono-3-oxobutanamide derivatives, *Arxivoc*, 17, 2008, 295.
8. Goyal RN, Verma MS, Singha NK, Voltammetric investigations of the reduction of direct orange-31 a bisazo dye, *Croatia Chem. Acta.*, 71(3), 1998, 715-726.
9. Park C, Lim J, Lee Y, Lee B, Kim S, Lee J, Kim S, Optimization and morphology for decolorization of reactive black 5 by *Funalia trogii*, *Enzy. Microb. Tech.*, 40, 2007, 1758-1764, DOI: 10.1016/j.enzymictec.2006.12.005.
10. Chandravadelu G, Senniappan P, *In-vitro* antimicrobial activity of novel derivative of azo dye from cyano ester, *Int. J. Res. Pharm. Chem.*, 1(4), 2011, 1082-1086.
11. Chopde HN, Meshram JS, Pagadala R, Mungole AJ, Synthesis, characterization and antibacterial activity of some novel azo-azoimine dyes of 6-bromo-2-naphthol, *Int. J. Chem. Tech. Res.*, 2(3), 2010, 1823-830.
12. Patel PS, Studies on synthesis and dyeing performance of disperse azo dyes based on Schiff base of ninhydrin and 3-amino phenol, *Arch. Appl. Sci. Res.*, 4(2), 2012, 846-851.
13. Swati G, Romila K, Sharma IK, Verma PS, Synthesis, characterization and anti- microbial screening of some azo compounds, *Int. J. Appl. Biol. Pharm. Tech.*, 2(2), 2011, 332-338.
14. Shridhari AH, Keshavayya H, Hoskeri HJ, RAS Ali, Synthesis of some novel bis 1,3,4-oxadiazole fused azo dye derivatives as potent antimicrobial agents, *Int. Res. J. Pure Appl. Chem.*, 1(3), 2011, 119-129, DOI: 10.9734/IRJPAC/2011/493.
15. Patil CJ, Patil Pooja A, Patil PB, and Patil Manisha C, Coupling Reactions Involving Aryldiazonium Salt: Part-I. Chemoselective Synthesis of 3-Oxo-(Substituted-2-phenylazo)-butyric acid ethylester derivatives and their Antibacterial Activity, *Der. Chemica. Sinica.*, 6(5), 2015, 108-114.
16. Patil CJ, Patil Manisha C, Pachpol NR and Waykole VS., Coupling Reactions Involving Aryldiazonium Salt: Part-II. Chemoselective Condensation with Acetylacetone and Antibacterial Activity, *Der. Chemica. Sinica.*, 6(5), 2015, 115-121.
17. Patil CJ, Patil Manisha C, Rane Vivek, Mahajan Kunal and Nehete CA, Coupling Reactions Involving Reactions of Aryldiazonium Salt: Part-III. Chemoselective Condensation with b-Naphthol to Synthesize Sudan-I, its Nitro Derivatives and Antibacterial Potential, *Int. J. Chem. Biol. Phy. Envir. Sci.*, (Communicated, June 2015).
18. Al-Rubaie LAR, Mhessn RJ, Synthesis and characterization of azo dye para red and new derivatives, *E-J. Chem.*, 9(1), 2012, 465-470, ISSN: 0973-4945.
19. Heinrich Z, *Color Chemistry: Syntheses, Properties and Applications of Organic Dyes and Pigments*, VCH, 2007, ISBN: 3906390233, 9783906390239.
20. Elisangela F, Andrea Z, Fabio DG, Cristiano RM, Regina DL, Artur CP, Biodegradation of textile azo dyes by a facultative *Staphylococcus arlettae* strain VN-11 using a sequential microaerophilic/aerobic process, *Int. Biodeter. Biodegrad.*, 63, 2009, 280-288.
21. Chakraborty A, Saha PK, Datta C, Synthesis and application of azo-naphthol dyes on wool, silk and nylon fabric, 7th Int. Conf. TEXSCI Sept., 2010, 6–8, Liberec, Czech. Rep.
22. Rathod KM, Thakre NS, Synthesis and antimicrobial activity of azo compounds containing m-cresol moiety, *Chem. Sci. Trans.*, 2(1), 2013, 25-28, DOI: 10.7598/cst2013.254.
23. Marmion DM, *Hand Book of Colorant*, Wiley, New York, 1991, ISBN: 0-471-50074-7.
24. Kenawy El-Refaie, Al-Deyab SS and Mohamed H, El-Newehy, Controlled Release of 5-Aminosalicylic Acid (5-AS A) from New Biodegradable Polyurethanes, *Molecules*, 75, 2010, 2257-2268, DOI: 10.3390/molecules15042257.
25. The Synthesis of Azo Dyes, <http://www2.unb.ca/chem/outreach/documents/AzoDyes.pdf> (referred on 05-02-2014).
26. Gosai DR, Nimavat KS, Vyas KB, Azo dyes based on salicylic acid-formaldehyde polymer as a polymeric ligands. *Der. Pharma. Chem.*, 3(4), 2011, 491-500.



27. Jerome J, Zalplky, Patel M.Dahylbhai, Heterocyclic Phenyl Azo Hydroxybenzenes., U.S. Patent, 4, 219, 474.
28. Raghavendra KR, Kumar K Ajay, Synthesis and Their Antifungal, Antihelmentic and Dying Properties of Some Novel Azo Dyes., Int. J. Pharma. Chem. Biol. Sci., 3(2), 2013, 275-280, ISSN: 2249-9504.
29. Karl H, Agback, Upsala, Sweden, Azo-bis-salicylic acid and salt thereof to treat inflammatory conditions of the Intestine, Patent Number, 4, 591, 584.
30. Evgenija Djurendic Sanja Dojcinovic Vujaskovic, Marija Sakac, Jovana Ajdukovic, Andrea Gakovic, Vesna Kojic, Gordana Bogdanovic, Olivera Klisuric and Katarina Penov Gasia, ARKIVOC, (ii), 2011, 83-102, Synthesis and biological evaluation of some new 2-oxazoline and salicylic acid derivatives.
31. Hrdina R, LuStinec D, Stolin P, Burgert L, Lunak S, Jr., Holdapek M, Iron Complexes of Reactive Azo Dyes., Adv. Colour Sci. Tech., 7(1), 2004, 6-17.
32. Patel BK, Prajapati NK, Patel DG, Synthesis, characterization and spectral study of chelating azo dyes containing salicylic acid ligand., Der. Chemica. Sinica, 4(6), 2013, 70-72.
33. Ewelina W. Eglarz-Tomczak, Łukasz Górecki, Azo dyes–Biological Activity and Synthetic Strategy. CHEMIK, 66(12), 2012, 1298-1307.
34. Abdu-Allah HHM, Abdel-Alim AM, Abdel-Moty SG, El-Shorbagi AA, Synthesis of Trigonelline and Nicotinamide Linked prodrugs of 5-Aminosalicylic Acid (5-Asa) With Analgesic and Anti-Inflammatory Effects, Bull. Pharm. Sci., Assiut University, 28(2), 2005, 237-253.
35. Lambert. HJ, Pitzele BS, Method and Compound For Testing Inflammatory Bowel Disease, U. S. Pat. No. 4312806, 26th Jan. 1982.
36. Popa S, Padure M, Jurcau D, Drutau M, Colour Study on Some Azoic Dyes Derived of Salicylic Acid, Chem. Bull. "Politehnica" Univ., (Timioara), 53(67), 2008, 1-2.
37. Bernt Jabes Lindberg, Amine addition salt of 5-[p-(2-pyridylsulphamyl)-phenylazo]-salicylic acid, U.S. Pat. No. 3,681,319, Application Ser. No. 603,437, Dec. 21, 1966.
38. Reddy M Prushotham, Prabhavathi K, Reddy, N. Rami, Reddy P Raveendra, Two simple spectrophotometric methods for the estimation of Mesalamine in Bulk sample and its pharmaceutical Dosage form, Global J. Pharmacol., 5(2), 2011, 101-105.
39. Henry Mirocourt, Manufacture of Chromaed Complexes of Azo and o-Hydroxy-azo Dye stuffs., US Patent No. 1,824,914, dated 29th Sept. 1931.
40. Garjani A, Davaran S., Rashidi M., Malek N, Protective effects of some azo derivatives of 5-aminosalicylic acid and their pegylated prodrugs on acetic acid-induced rat colitis., Daru J. Pharm. Sci., 12, 2004, 24.
41. Marc E, Broe De, Stolar Jean-Claude, Etienne J. Nouwen, Monique M. Elseviers, 5-Aminosalicylic Acid and Chronic interstitial Nephritis, Clinical Nephrotoxins, part-B 1998, 217-222 DOI:10.1007/978-94-015-9088-4_15.
42. Kracker Herbert, Azo-dyestuffs, US Pat No. 2690438, dated 28 Sept. 1954.
43. Jilani JA, Shomaf M, Alzoubi KH, Synthesis and Evaluation of Mutual Azo Prodrug of 5-Aminosalicylic acid linked to 2-Phenylbenzoxazole-2-yl-5-acetic acid in Ulcerative Colitis., Drug Design, Develop. and Therapy, 7, 2013, 691–698.
44. Anders Askelof EE, Svartz N, Carlo H, Willstaedt, US Pat. 2,396,145, 5th Mar. 1946, Uppsala Sweden, Assignors to Aktiebolaget Pharmacia; Stookholm, Sweden, a registered company, Heterocyclic Sulphonamido Azo Compounds.
45. Ju He, Xia Tao, Wanhong Ma, and Jincai Zhao, Chemistry Letters, (2001) 86-88, Heterogeneous Photo-Fenton Degradation of an Azo Dye in Aqueous H₂O₂/Iron Oxide Dispersions at Neutral pHs.

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