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Synthesis of New Disperse Dyes Based on Enaminones Derivatives: Part 3. In vitro cytotoxic activity

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Abstract

After preparing a series of new dispersed dyes based on enaminone derivatives, verifying the validity of the chemical compositions using the latest modern scientific methods, studying them, and publishing the results that indicate the effectiveness of these new dispersed dyes against a group of bacteria and cancer cells. In this study we evaluated the cytotoxic effects of the synthesized dyes using the normal cell line, lung WI-38, where the dyes showed satisfactory results and are promising towards their safe use on human lung fibroblast normal cells WI-38. As anti-proliferative agents with good selectivity index range (1.65–6.42), the dyes 5a–5f under investigation shown non-significant cytotoxic impact with CC50 values of 7.71, 24.49, 21.01, 104.51, 33.74, and 115.67 mM, respectively. These results provided a favourable safety profile.

***Keywords*:** human lung fibroblast normal cells WI-38, enaminones, *disperse dyes*

1. Introduction

One important family of organic chemicals that is widely used in many industrial and pharmacological applications are heterocyclic derivatives [1-29]. Enaminone derivatives are among the most important heterocyclic compounds in medical chemistry [1-3, 7, 18-20]. Disperse dyes are considered one of the most important industrial dyes that are used in dyeing synthetic fibers, such as polyester.

These dyes are poorly soluble in water and can be easily prepared, so they are widely used. For one or more hydrophobic fibres, such as cellulose acetate, nylon, polyester, acrylic, and other synthetic fibres, dispersion dyes exhibit substantivity. Since there is no way to lessen the negative charge on the surface of hydrophobic fibres like polyester, non-ionic dyes like dispersion dyes are employed instead, since they are unaffected by the surface charge [1. 2]. The phrase "disperse dye" refers to organic colouring agents that are suited for dyeing hydrophobic fabrics, have a low water solubility, and are free of ionising groups. Because of its insoluble aqueous characteristics and requirement to be applied from an aqueous dispersion, the dye got its name. They have the shortest molecular size of all the dyes. Pigments are unsaturated organic chemical compounds that are coloured and have the ability to colour or dye a substrate, such as textiles. One kind of dye used to colour synthetic fibres like acrylic, polyester, and nylon is called a dispersion dye. Water-insoluble disperse dyes are applied to the fibres as minuscule particles that are dispersed uniformly throughout the cloth. These dyes, which are widely used in the textile industry to create a variety of clothing and other products, are renowned for their vivid and strong colours. We examined their antiproliferative effects on the colon cancer cell line HCT-116, the breast adenocarcinoma cell line MCF-7, the lung cancer cell line A-549, and the hepatocellular carcinoma cell line HepG-2 in our published work [1. 2]. In this study, we will review the added value of these new dyes by presenting their properties towards normal cells and whether they have a harmful effect on them or can they be used in a safe manner.

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2. Materials and Methods

Preparation of Disperse Dyes

Some novel disperses dyes were synthesized accordingly with our published paper based on enaminones. [1].

Evaluation of Cytotoxic Effects of dyes 5a-5f

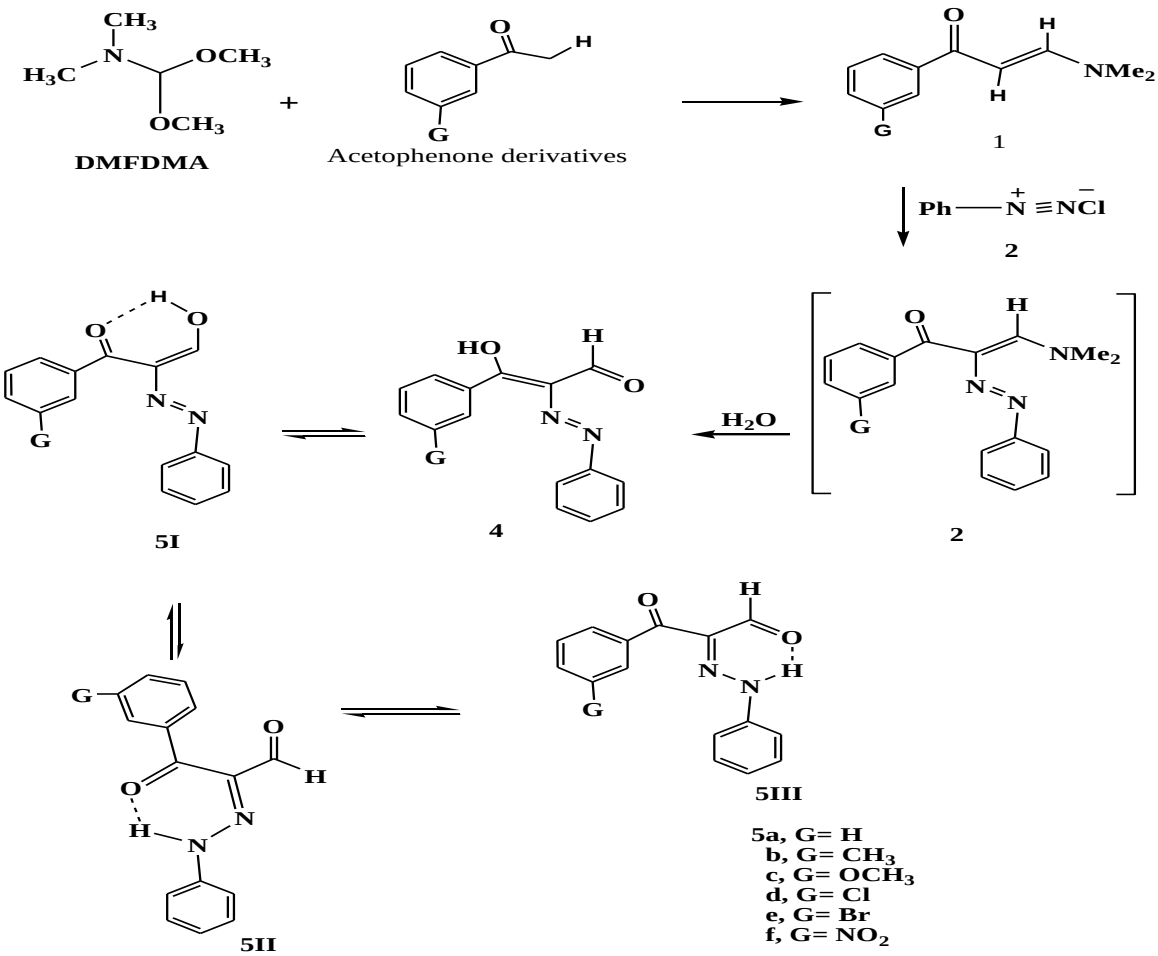
Mammalian cell lines: The American Type Culture Collection (ATCC, Rockville, MD) provided the human lung fibroblast normal cells, or WI-38 cells. Chemicals Used: Sigma (St. Louis, Mo., USA) provided the trypan blue dye, MTT, and dimethyl sulfoxide (DMSO). Lonza (Belgium) supplied the foetal bovine serum, DMEM, HEPES buffer solution, L-glutamine, gentamycin, and 0.25% Trypsin-EDTA.

Cell line Propagation:

The cells were cultured in Dulbecco's modified Eagle's medium (DMEM), which was enhanced with 50µg/ml of gentamycin, 10% heat-inactivated foetal bovine serum, 1% L-glutamine, and HEPES buffer. Every cell was subcultured twice a week and kept at 37ºC in a humidified environment with 5% CO_2.

3. Result and discussion

Some novel disperses dyes were synthesized accordingly with our published paper based on enaminones. (Scheme 1) [1. 2]. The capacity of dyes, 5a–5f, to cause cytotoxicity against the human normal lung fibroblast cell line (WI-38 cells) was assessed. Table 1 presented the results, represented as (IC50) values, along with the computed selectivity index.



Scheme 1: Chemical structures of dyes [1].

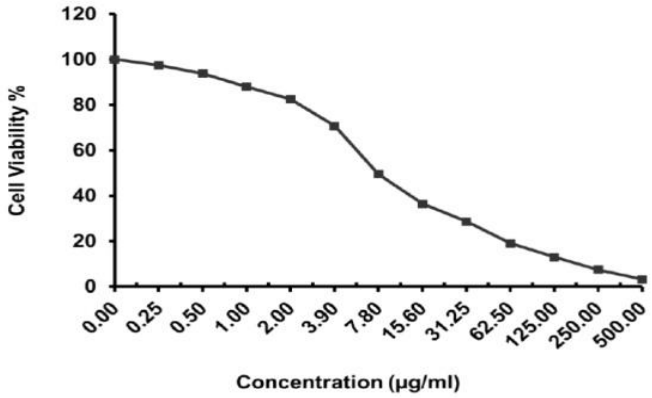
Cytotoxic Activity towardNormal Human WI-38

To determine if the synthetic disperse dyes could be utilized on normal cells without causing harm, the cytotoxic impact of disperse dyes **5a**–**5f** was evaluated against the normal human lung cell line (WI-38). IC_{50} values were used to express the results (see Table 1 and Figure 1-6).

Disperse dyes **5a**, **5b**, **5c**, 5d, **5e**, and **5f**, with corresponding CC_{50} values of 7.71, 24.49, 21.01, 104.51, 33.74, and 115.67, were found to have a non-noteworthy cytotoxic effect on WI-38 cells.

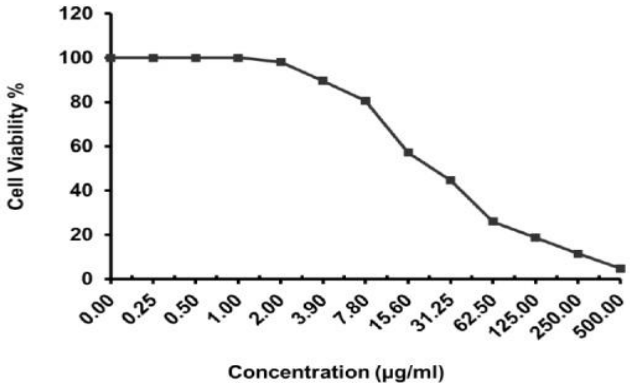
Table 1. Cytotoxic activity of dyes 5a-f on normal normal human lung cell line (WI-38).

Dye No.	(CC_{50} µg/mL) Lung WI-38	Selectivity Index			
		MCF-7	HCT-116	A-549	HepG-2
5a	7.71± 0.64	1.96	3.99	2.67	4.45
5b	24.49± 2.69	3.28	3.60	3.45	6.13
5c	21.01± 2.37	3.08	5.66	5.75	6.42
5d	104.51 ± 5.97	2.87	3.11	3.66	4.57
5e	33.74± 3.04	2.39	2.78	3.65	5.13
5f	115.67 ± 6.21	2.74	2.11	1.91	1.65



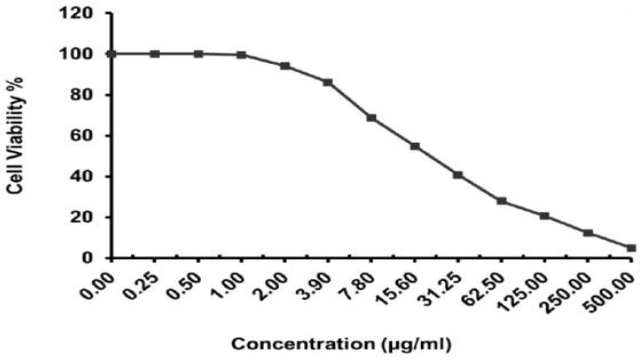
Sample conc. (µg/ml)	Viability %	Inhibitory %	S.D. (±)
500	3.18	96.82	0.06
250	7.46	92.54	0.82
125	12.95	87.05	0.71
62.5	19.08	80.92	1.46
31.25	28.63	71.37	0.95
15.6	36.48	63.52	1.68
7.8	49.52	50.48	1.49
3.9	70.68	29.32	2.46
2	82.49	17.51	0.35
1	88.03	11.97	1.09
0.5	93.81	6.19	0.73
0.25	97.46	2.54	0.12
0	100	0	

Figure 1. WI-38 human lung fibroblast normal cells for dye 5a.



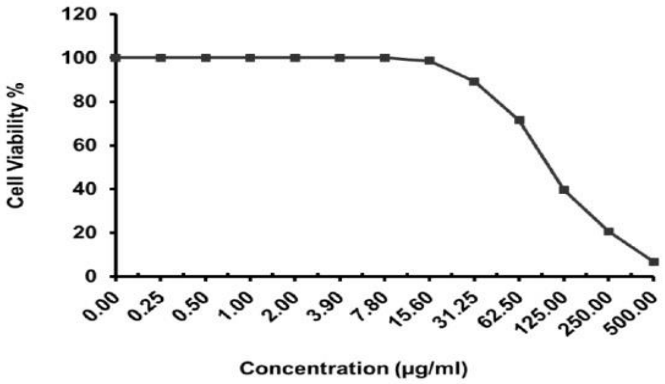
Sample conc. (µg/ml)	Viability %	Inhibitory %	S.D. (±)
500	4.76	95.24	0.32
250	11.42	88.58	0.69
125	18.78	81.22	1.64
62.5	25.91	74.09	1.37
31.25	44.62	55.38	2.84
15.6	57.13	42.87	3.51
7.8	80.46	19.54	2.02
3.9	89.52	10.48	1.65
2	98.07	1.93	0.69
1	100	0	
0.5	100	0	
0.25	100	0	
0	100	0	

Figure 2. WI-38 human lung fibroblast normal cells for dye 5b.



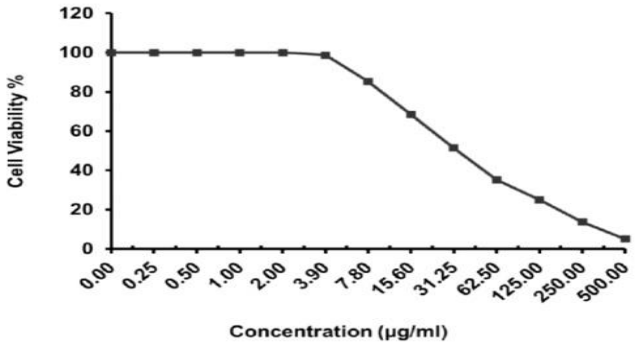
Sample conc. (µg/ml)	Viability %	Inhibitory %	S.D. (±)
500	4.95	95.05	0.37
250	12.37	87.63	1.09
125	20.62	79.38	0.84
62.5	27.87	72.13	1.95
31.25	40.78	59.22	2.06
15.6	54.90	45.1	1.42
7.8	68.75	31.25	2.13
3.9	86.19	13.81	1.37
2	94.23	5.77	0.15
1	99.56	0.44	0.22
0.5	100	0	
0.25	100	0	
0	100	0	

Figure 3. WI-38 human lung fibroblast normal cells for dye 5c.



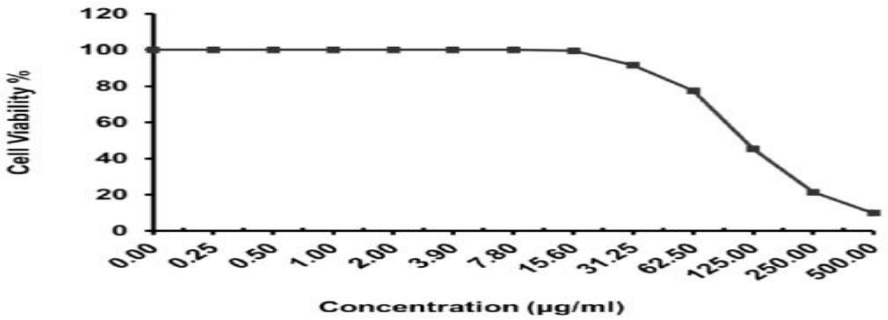
Sample conc. (µg/ml)	Viability %	Inhibitory %	S.D. (±)
500	6.72	93.28	0.44
250	20.63	79.37	0.79
125	39.54	60.46	2.31
62.5	71.45	28.55	1.57
31.25	89.15	10.85	2.03
15.6	98.64	1.36	0.82
7.8	100	0	
3.9	100	0	
2	100	0	
1	100	0	
0.5	100	0	
0.25	100	0	
0	100	0	

Figure 4. WI-38 human lung fibroblast normal cells for dye 5d.



Sample conc. (µg/ml)	Viability %	Inhibitory %	S.D. (±)
500	5.03	94.97	0.11
250	13.78	86.22	0.64
125	24.96	75.04	1.72
62.5	35.12	64.88	2.06
31.25	51.29	48.71	2.37
15.6	68.41	31.59	1.35
7.8	85.24	14.76	0.68
3.9	98.76	1.24	0.42
2	100	0	
1	100	0	
0.5	100	0	
0.25	100	0	
0	100	0	

Figure 5. WI-38 human lung fibroblast normal cells for dye 5e.



Sample conc. (µg/ml)	Viability %	Inhibitory %	S.D. (±)
500	9.87	90.13	0.61
250	21.43	78.57	1.59
125	45.18	54.82	2.44
62.5	77.48	22.52	1.86
31.25	91.47	8.53	0.65
15.6	99.65	0.35	0.09
7.8	100	0	
3.9	100	0	
2	100	0	
1	100	0	
0.5	100	0	
0.25	100	0	
0	100	0	

Figure 6. WI-38 human lung fibroblast normal cells for dye 5f.

According to Badisa *et al.* and others [x], a drug's selective index value greater than two indicates specific toxicity to cancer cells. On the other hand, a chemical is considered typically dangerous if its selective index value is less than two, indicating that it can cause cytotoxicity in normal cells. The anticancer medications dispersion dyes 5a, 5b, 5c, 5d, 5e, and 5f demonstrated an excellent range of 2.11 to 6.42 and a high selectivity index (WI-38/MCF-7), WI-38/HCT-116, WI-38/A-549, and WI-38/HepG-2. The 5F dye's selectivity index values against A-549 and HepG-2 were 1.91 and 1.65, respectively, with some slight variations.

4. Conclusions

The results indicated the efficacy of these novel dispersion dyes against a range of cancer cells. The cytotoxic effects of the dyes were also assessed using the normal cell line, and the dyes demonstrated good anticancer agents. In conclusion, no significant cytotoxic impact was observed by any of the active equivalents 5a–5fi when tested for cytotoxicity against the normal human cell line, WI-38 lung fibroblast, indicating an excellent safety profile.

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