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The evaluation of 5-fluorouracil toxicty on *Corbicula striatella* (Deshayes, 1830)

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Abstract
The calculation of toxicity evaluation LC10 and LC50 values for 24 and 96 hours. In present study, the toxicity of 5- Fluorouracil on *Corbicula striatella*. It is allow that which is the increasing time of concentration, mortality rate will be increased. This investigation the accurate sources of their death is not known but it is proved that 5-Fluorouracil brings some changes in physiochemical properties of water and it affects the metabolic as well as physiological rate leading to the death of animals. The toxicity study provides the level of safe concentration of toxicant.

Keywords: *Corbicula striatella*, 5-fluorouracil, toxicity

Introduction
In oceanic water comprises over 70% of the earth's surface covered by water is most precious natural resource that exists on our planet. Without the seemingly invaluable compound compromise of hydrogen and oxygen, the life on earth would be non-existent, it essential for everything on our planet to grow proper. Subsequently, we are slowly but surely harming our planet to the point where organisms are dying at very alarming rate. In addition to innocent organism dying off, our drinking water has become greatly affected as is our ability to use water for recreational purposes. 5-Fluorourasil is the anticancer drug and is used as multidrug administration in vitro in the human breast cancer cell line. This drug induced 60% cell death at 5 µg/ml dose. It is also sometimes used to induce apoptosis. In order to test the hypothesis that elemental diets protect the intestinal mucosa against 5-fluorouracil toxicity, (Jane 1983) [4]. Cytoplasmic peptide hydrolase activities and mucosal DNA contents were also severely decreased after 5-fluorouracil injection, the changes observed being independent of the di*et. al*so, none of the elemental diets reduced the body weight losses observed after 5-fluorouracil administration. Although the effects of the sodium salt of 5-fluorouracil on body weight and food intakes were much less severe than those of the Tris salt. Results do not support the suggestion that elemental diets might reduce the intestinal toxicity of 5-fluorouracil.

Materials and Methods
The method described by Finney (1951), Medium sized bivalves, Corbicula striatella were collected from the Girna Dam near Chalisgaon city, M.S. India, latitude 200 28' 58" N, longitude 740 43' 13" E and brought to the laboratory. The room temperature was 23 ^{0}C – 26 ^{0}C and the pH of water was in the range of 7 – 8. Lethal toxicity tests were conducted over 96 hours. The experimental troughs containing 5 liters dechlorinated water were used to expose the animals. Stock solutions of 5-fluorouracil were prepared in double glass-distilled water and added to the test medium to get the desired concentration. Ten animals were exposed to 10 – 12 different concentrations of heavy metals. After every 12 hours, the water was changed by the fresh solution of the same concentration of c 5-fluorouracil. Dead bivalves were counted individually. The resulting mortality was noted in the range of 10 to 90 % for each concentration for the duration of 24, and 96 hrs. Each experiment was repeated thrice till constant results were obtained.
Acute toxicity tests were carried out under static conditions up to 96 hours. The data collected was then analyzed statistically by means of the Probit method on transforming the toxicity curve (% mortality versus log of Conc.) into regression lines (Mortality in Probit / log Conc.) which allows the average medium lethal concentration of LC50 to be calculated for 24 and 96 hrs.

Discussion
Experiments during recent years have shown that higher dose of anticancer drug compounds are injurious to molluscs. Further, in the extremely low concentration level of these

substances, the bivalves and other organisms in aquatic environment are exposed for as long as they persist in the medium. The evaluation of LC50 concentrations of anticancer drugs or toxicant is the first step before carrying further studies on physiological changes in animals Anticancer drugs, 5- fluorouracil effective antitumour agents utilized in the treatment of a wide variety of malignancies. Nuclear transfer technology (Campbell 1999; Prather *et.al*., 1999; Gomez *et.al*., 2003) [1, 9, 3], in studies of the cell cycle, the most frequently measured attribute is DNA content, whereby this marker indicates cell maturity in the cycle. The identification of a relatively highly proliferative tissue type from bivalves could be relevant across molluscan taxa and will contribute to the attempts being made at establishing cell culture lines from oysters or bivalves in order to delineate disease pathogenesis mechanisms. Moreover, the choice of an actively dividing tissue is useful in cytogenetics, for examining proliferation as a biomarker because of stressor impacts in feral oysters, and for assessing proliferative or non proliferative influences of chemical compounds. Different tissues of complex multicellular organisms are composed of cells having characteristic morphologies, with each tissue having its own growth properties (Tapon *et. al*., 2001) [11]. The proliferative capability of cells derived from specific organs of bivalves has been studied, as has that of cells from digestive gland (Marigomez *et.al*., 1999) [6] and gill cells from mussels (Gomez-Mendikute *et. al*., 2005; Sollid *et. al*., 2005) [10]. The identification of a relatively highly proliferative tissue type from bivalves could be relevant across molluscan taxa and will contribute to the attempts being made at establishing cell culture lines from oysters in order to delineate disease pathogenesis mechanisms. Moreover, the choice of an actively dividing tissue is useful in cytogenetics, for examining proliferation as a biomarker because of stressor impacts in feral oysters, and for assessing proliferative or non proliferative influences of chemical compounds. The pyrimidine analog 5-fluorouracil is still one of the most useful antitumour agents for treatment of solid cancers (Longley *et. al*. 2003) [5]. In spite of this, its mechanism of action is still not fully understood. Thymidylate synthase is thought to be one important target of 5-5-fluorouracil (Parker and Cheng 1990) [7]. The 5-Fluorouracil plays an important role in the systemic treatment of various solid tumors, such as gastrointestinal cancer, breast cancer, and head and neck cancer. Extensive knowledge has been acquired on the metabolic pathways and mechanism of action of 5-FU. (Pinedo and Peters, 1998) [8].

Observation tables

Calculation of LC10 and LC50 values

Calculation of LC10 and LC50 5-fluorouracil calculated from regression equation Y = 3.7184 and Y = 5.00 (values from Finney's Table 1) were used to calculate LC10 and LC50 values in ppm of 5-fluorouracil respectively for 24 and 96 hours.

Calculation of percent morality

Abbots formula (1925) was used for getting the exact morality due to toxicant as below.

$$P = \frac{Om - Cm}{100 - Cm} \times 100$$

Where,

P - Corrected mortality
Om - Observed mortality
Cm - Control mortality
(All percentages)

It was observed that there was no mortality in control group of bivalves. The mortality data obtained in experimental set of bivalves for each dose was calculated by Finney's formula.

$$P = \frac{r}{n} \times 100$$

Where,

P - Percentages mortality
r - Mortality observed
n - Number of animals exposed in batch.

Results

The mortality data thus obtained was put into empirical probit / log concentration to plot Probit regression lines. The 50% mortality and 10% mortality causing *Corbicula striatella* were to5-fluorouracil. Static acute toxicity test were carried out in the laboratory condition until 96 hours duration for 5-fluorouracil. Toxicity test were conducted for 24 and 96 hrs by the method described by Finney (1951). The regression equations were obtained for 5-fluorouracil. The result obtained after toxicity evaluation of 5-fluorouracil on *Corbicula striatella* are cited in tables 1. To 2.

The LC10 and LC50 values for 5-fluorouracil are 4.2257 ppm respectively. The LC10 values for 24 and 96 hrs are 3.193 and 31.39 ppm respectively. The LC50 values for 24 and 96 hrs exposures to 5-fluorouracil for 24 and 96 hrs are 10.58 and 37.16 ppm respectively.

Conclusion

5-Fluorouracil is the anticancer drug safe and minimum dose are useful to treatment of animals otherwise excess or high dose are harmful. 5- fluorouracil to inhibit the extra mass of malignancies such as dose depends upon the animal body structure. Safe dose to prevent the abnormal growth of cells or apoptosis. High dose are regulate toxicity of animal get increase mortality.

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Table 1: Calculation of Regression equation for LC_{10} and LC_{50} values of *Corbicula striatella* exposed to 5-fluorouracil for 24 hrs.

Sr. No.	Conc. of 5-FU (PPM)	Log of conc. to base 10 'x'	No. of bivalves exposed 'n'	Morta-lity for 24hrs. 'r'	% mortality P=(100.r)/n	Empirical probit 'X'	Expected probit 'Y'	Weighing coefficient 'w'	Weight W=nw	Working probit 'y'	Wx	Wy	Wx^2	Wy^2	Wxy	Improved expected probit 'Y'
I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV	XV	XVI	XVII
1	2.5	0.3979.	10	1	10	3.7184	3.25	0.17994	1.7994	4.012	0.7159	7.2191	0.2848	28.9630	2.8721	3.45
2	5.0	0.6989	10	2	20	4.1584	4.15	0.47144	4.7144	4.160	3.2948	19.6119	2.3027	81.5855	13.7063	4.19
3	7.5	0.8790	10	3	30	4.4756	4.67	0.60052	6.0052	4.479	5.2545	26.8972	4.5971	120.4725	23.5349	4.64
4	10.0	1.0000	10	4	40	4.7467	5.02	0.63662	6.3662	4.749	6.3642	30.233	6.3662		30.2330	4.93
5	12.5	1.0969	10	5	50	5.0000	5.22	0.62742	6.2742	4.997	6.8821	31.3521	7.5489	156.6664	34.3898	5.17
6	15.0	1.1760	10	7	70	5.5244	5.52	0.58099	5.8099	5.524	6.8324	32.0938	8.0349	177.2861	37.7421	5.37
7	17.5	1.2430	10	8	80	5.8416	5.77	0.53159	5.3159	5.834	6.6076	31.0129	8.2132	180.9292	38.5487	5.53
									∑W=36.2852		∑Wx=35.9535	∑Wy=178.4200	$\sum Wx^2$=37.3483	$\sum Wy^2$=889.4794	∑Wxy=181.0272	

1. $\bar{x} = \frac{\sum Wx}{\sum W} = \frac{35.9535}{36.2852} = 0.9908$

2. $\bar{y} = \frac{\sum Wy}{\sum W} = \frac{178.4200}{36.2852} = 4.9171$

3. $b = \frac{\sum Wxy - \bar{x}.\sum Wy}{\sum Wx^2 - \bar{x}.\sum Wx} = \frac{181.0272 - (0.9908) \times 178.4200}{37.3483 - (0.9908) \times 35.9535} = \frac{4.2486}{1.7255} = 2.4622$

LC_{50} i.e. $X = \frac{5 + (b\bar{x} - \bar{y})}{b}$ $LC_{10} = \frac{5 + (b\bar{x} - \bar{y})}{b}$

$= \frac{5 + (2.4622 \times 0.9908) - 4.9171)}{2.4622}$

Anti log of 1.0244 Anti log of=0.5039

∴ LC_{50} = 10.58 LC_{10}= 3.193

Regression equation

4. $Y = \bar{y} + b(X - \bar{x})$ $= 4.9171 + 2.4622X - 2.4622 \times 0.9908$

$= 2.4622X - 2.4775$

Table 2: Calculation of Regression equation for LC_{10} and LC_{50} values of *Corbicula striatella* exposed to 5-fluorouracil for 96 hrs.

Sr. No.	Conc. of 5-FU mg/lit	Log of Conc. to base 10 'x'	No. of animal exposed 'n'	Mortality 96 hours 'r'	Percentage mortality p=(100r)/n	Empi-rical probit	Expe-cted probit 'Y'	Weigh-ing coeffic-ient 'w'	weight W=nw	work-ing probit 'y'	Wx	Wy	Wx^2	Wxy	Wy^2	Improved expected probit y
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1	33	1.5185	10	2	20%	4.1584	4.15	0.47144	4.7144	4.160	7.158816	19.611904	10.870	29.780	81.858	4.095
2	36	1.5563	10	4	40%	4.7467	4.80	0.62742	6.2742	4.747	9.764537	29.783627	15.196	46.352	141.382	4.757
3	39	1.5910	10	6	60%	5.2553	5.45	0.60052	6.0052	5.250	9.554273	31.5273	15.200	50.159	165.518	5.365
4	41	1.6127	10	8	80%	5.8416	5.84	0.50260	5.0260	5.841	8.105430	29.356866	13.0715	47.3438	171.473	5.745
5	44	1.6434	10	9	90%	6.2816	6.29	0.37031	3.7031	6.278	6.085674	23.248062	10.000	38.205	145.951	6.283
6	47	1.6720	10	10	100%	--	--	--	--	..	--	--	--	--	--	--
									SW= 25.7229		SWx= 40.66873	SWy= 133.52776	SWx^2= 64.340	SWxy= 211.84255	SWy^2= 705.911	

i. $\bar{x} = \frac{SWx}{SW} = \frac{40.66873}{25.7229} = 1.5810321$ iv. $Y = \bar{y} + b(x - \bar{x})$

ii. $\bar{y} = \frac{SWy}{SW} = \frac{133.52776}{25.7229} = 5.1910072$

$= 5.1910072 + 17.518833 (x – 1.5810321)$

$= 5.1910072 + 17.518833x – 27.697337$

$= 17.518833 x - 22.50683$

iii. $b = \frac{SWxy - x.SWy}{SWx^2 - x.SW}$

$= \frac{211.84255 - 1.5810321 \times 133.52776}{64.340287 – 1.5810321 \times 40.66873}$

$LC_{10} = \frac{3.7184 + 22.50683}{17.518833} = 1.4969$ Antilog = 31.39

$LC_{50} = \frac{5.0 + 22.50683}{17.518833} = 1.5701$ Antilog = 37.16

$= \frac{211.84255 - 211.11167}{- 64.29856} = \frac{0.7308752}{0.0417194} = 17.518833$

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