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EVALUATION OF ANTI-MITOTIC ACTIVITY OF INDOLE DERIVATIVE ON GERMINATING BENGAL GRAM SEEDS

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ABSTRACT

Isatin and its analogs are versatile substrates, which can be used for the synthesis of numerous heterocyclic compounds. Isatin and its derivatives are used in organic synthesis and they are used in evaluating new product that possesses different biological activities. The synthetic versatility of Isatin derivatives has been draw the attention in several synthetic organic and medicinal chemists due to varied biological and pharmacological properties of such compounds. Literature survey revealed that isatin (1H-indole-2,3-dione) possesses diverse chemotherapeutic activities, such as anticancer (Gursoy and Karal, 2003), antiviral (Debra et al., 2006), anti-HIV (Pandeya et al., 1999a), anti-mycobacterial (Karal et al., 2007), antibacterial (Pandeya et al., 1999b), anti-inflammatory (Sridhar and Ramesh, 2001) and anticonvulsant (Verma et al.,2004). Among these properties, cytotoxic and antiproliferative activities of this moiety have been found to be interesting.

KEYWORDS: Cancer is one of the most complicated diseases across the world wide.

INTRODUCTION

Isatin and its analogs are versatile substrates, which can be used for the synthesis of numerous heterocyclic compounds. Isatin and its derivatives are used in organic synthesis and they are used in evaluating new product that possesses different biological activities. The synthetic versatility of Isatin derivatives has been draw the attention in several synthetic organic and medicinal chemists due to varied biological and pharmacological properties of such compounds. Literature survey revealed that isatin (1H-indole-2,3-dione) possesses diverse chemotherapeutic activities, such as anticancer (Gursoy and Karal, 2003), antiviral (Debra et al., 2006), anti-HIV (Pandeya et al., 1999a), anti-mycobacterial (Karal et al., 2007), antibacterial (Pandeya et al., 1999b), anti-inflammatory (Sridhar and Ramesh, 2001) and anticonvulsant (Verma et al.,2004). Among these properties, cytotoxic and antiproliferative activities of this moiety have been found to be interesting. It has been reported in the literature that compounds bearing 1,3,4-oxadiazole ring possess significant biological properties such as anticancer (Aboraia et al., 2006), anti-inflammatory (Nargund et al., 1994), antiviral (Kucukguzel et al., 2007) activities. In view of the biological importance of these isatin or indole derivatives, we have selected 1-(4-Chlorobenzylidene)-5-(2-oxoindolin-3-ylidene) Thiocarbohydrazone for possible evaluation for the antimitotic activity.

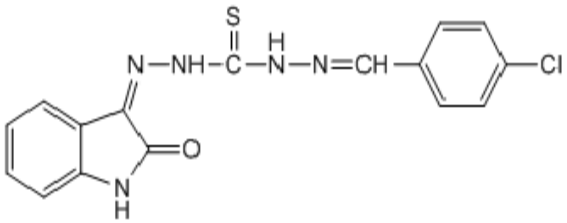
Cancer is one of the most complicated diseases across the world wide. Most of the anticancer or chemotherapeutic drugs act by interrupting cell division (mitosis) in fast-dividing cells. The inhibition of mitosis in gram seed root tip is considered as a sensitive and easy method for the determination of cytotoxicity of drugs (Thenmozhi et al., 2011) [(4)]. A study about the inhibition of mitosis in gram seeds proved that there is a disturbance in the mitotic spindle formation and also inhibition of cell plate formation which may be due to the arrest of cell division at G2 phase or S phase (Yuet et al., 2012). The inhibition of mitosis by the test compound is beneficial for their possible applications for life-threatening diseases such as cancer. In view of above, we have planned to evaluate the anti-mitotic activity of test compound i.e. 1-(4-Chlorobenzylidene)-5-(2-oxoindolin-3-ylidene) Thiocarbohydrazone using germinating Bengal gram seed methods.

MATERIALS AND METHODS

Bengal Gram Seeds: The high quality germinating bengal gram seeds were purchased from local market for the evaluation of anti-mitotic activity.

Bengal gram seeds used for the study

Test compound: 1-(4-Chlorobenzylidene)-5-(2-oxoindolin-3-ylidene) Thiocarbohydrazone was selected for the evaluation of antimitotic activity using bengal gram seeds and its synthesis, characterization, antioxidant and antimicrobial activity of this compound was reported (Kiran et al., 2013). The compound is solubilized in dimethyl sulfoxide (DMSO) and is insoluble in water.



Name: 1-(4-Chlorobenzylidene)-5-(2-oxoindolin-3-ylidene) Thiocarbohydrazone

The Physical data of the above selected compound is presented in Table 1.

Table 1: Physical data of the selected compound.

Molecular formula	Molecular weight	Melting point	% yield
$C_{16}H_{12}ClN_5OS$	357	138–140 ^{0}C	54

Preparation of test suspension: As the compound is insoluble in water, we prepared suspension of test compound to evaluate the anti-mitotic activity using standard methods and gum tragacanth was used as suspending agent. A test concentration of 1, 2 and 5 mg/ml were prepared and used for the study.

Anti-mitotic activity: Bengal gram seeds of a good quality were taken and soken overnight with water to hasten the germination process. The next day the seeds were distributed in a group of 10 each in Petri dishes on moistened filter paper. Drug suspensions were prepared at concentrations of 1, 2 and 5 mg/ml and added to the filter paper in the Petri dishes. One Petri dish served as control without test sample, and other served as test samples. The seeds were allowed to germinate for 4 days and care was taken to moisten the filter paper with control and drug solutions every 24 hours. The length of the radicals was measured in cm at the end of 4th day and calculated the % growth inhibition.

Statistical analysis: All the experimental values were expressed as mean ± SD (N=10). One-way analysis of variance (ANOVA) and Dunnett's test were used to compare means from the control group and each of the test groups and the statistical significance was judged at the 0.05 probability level.

RESULTS AND DISCUSSION

In the present study, we have evaluated the antimitotic activity of newly synthesized isatin derivative i.e. 1-(4-Chlorobenzylidene)-5-(2-oxoindolin-3-ylidene) Thiocarbohydrazone using germinating Bengal gram seeds. The test compound showed the antimitotic activity with different concentrations and was found to be as dose dependent manner. The results were showed in table 2.

Table 2: Anti-mitotic activity of test compound.

Anti-mitotic Activity of test compounds				
	Length of the radical of bengal gram seeds (in cm)			
	Control	Test 1mg/ml	Test 2 mg/ml	Test 5 mg/ml
	3.2	2	1.5	1.2
	3.93	1.7	1	1
	3.41	1.2	0.8	0.9
	3.5	1.2	1.2	0.9
	4.15	1.4	1.8	0.7
	3.61	1.4	1.2	0.8
	4.21	1.5	1.3	1
Mean	3.72	1.49	1.26	0.93
SD	0.39	0.29	0.33	0.16
% inhibition		60.02	66.17	75.01
p value		<0.001	<0.001	<0.001

P values are expressed in comparison with control; n=10

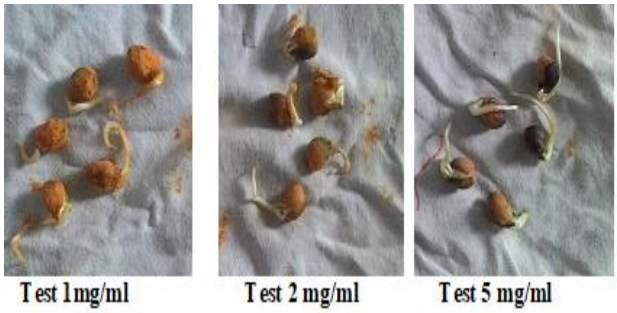


Figure 1: Images showing the germination of Bengal gram seeds in presence of different concentrations of test compound.

The test compound is capable of inhibiting the germination of Bengal gram seeds 60.02%, 66.17% and 75.01% with the doses of 1, 2 and 5 mg/ml respectively indicating the potential anti-mitotic activity of the test compound. In present study, the test compound showed significant effect as anti-mitotic in comparison with the control and this is benefit result for inhibiting the growth of cancer cells.

The biochemical similarity between plants and animals can be exploited to use plants as an alternative system for animal experiments for the development of new drugs (Nayak and Lakshmi, 2014). Growth inhibition assays in plants provide another better way of detecting the anti-mitotic potential of various drugs (Alamgir et al., 2014). Germination of Bengal gram seeds and A. cepa test are the two common methods used to test anti-mitotic activity (Nayak and Lakshmi, 2014). Most of the chemotherapeutic drugs act by interrupting cell division (mitosis) in fast-dividing cells. The inhibition of mitosis in gram seed root tip is considered as a sensitive and easy method for the determination of cytotoxicity of drugs (Thenmozhi et al., 2011).

A study about the inhibition of mitosis in gram seeds proved that there is a disturbance in the mitotic spindle formation and also inhibition of cell plate formation which may be due to the arrest of cell division at G2 phase or S phase (Yuet et al., 2012). The inhibition of mitosis by the test compound is beneficial for their possible applications for life-threatening diseases such as cancer. Thus, we suggest that the cytotoxic action of test compound can involve disturbance of mitotic processes in the fast-dividing cancer cells which will be beneficial for cancer management. Our samples, being capable of arresting the mitotic progression of plant cells; it may have the potential to find opportunities in arresting the cancer cell proliferation. More studies are required on the cellular and the molecular levels of animals (both in vitro and in vivo) to correlate these aspects with the cancer biology.

CONCLUSIONS

In conclusion, the present study results proved that the test compound is having potent anti-mitotic activity against the germinating gram seed method. The inhibition of mitosis by the test compound is beneficial for their possible applications for life-threatening diseases such as cancer. Thus, we suggest that the cytotoxic action of test compound can involve disturbance of mitotic processes in the fast-dividing cancer cells which will be beneficial for cancer management.

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