

SHORT COMMUNICATIONS

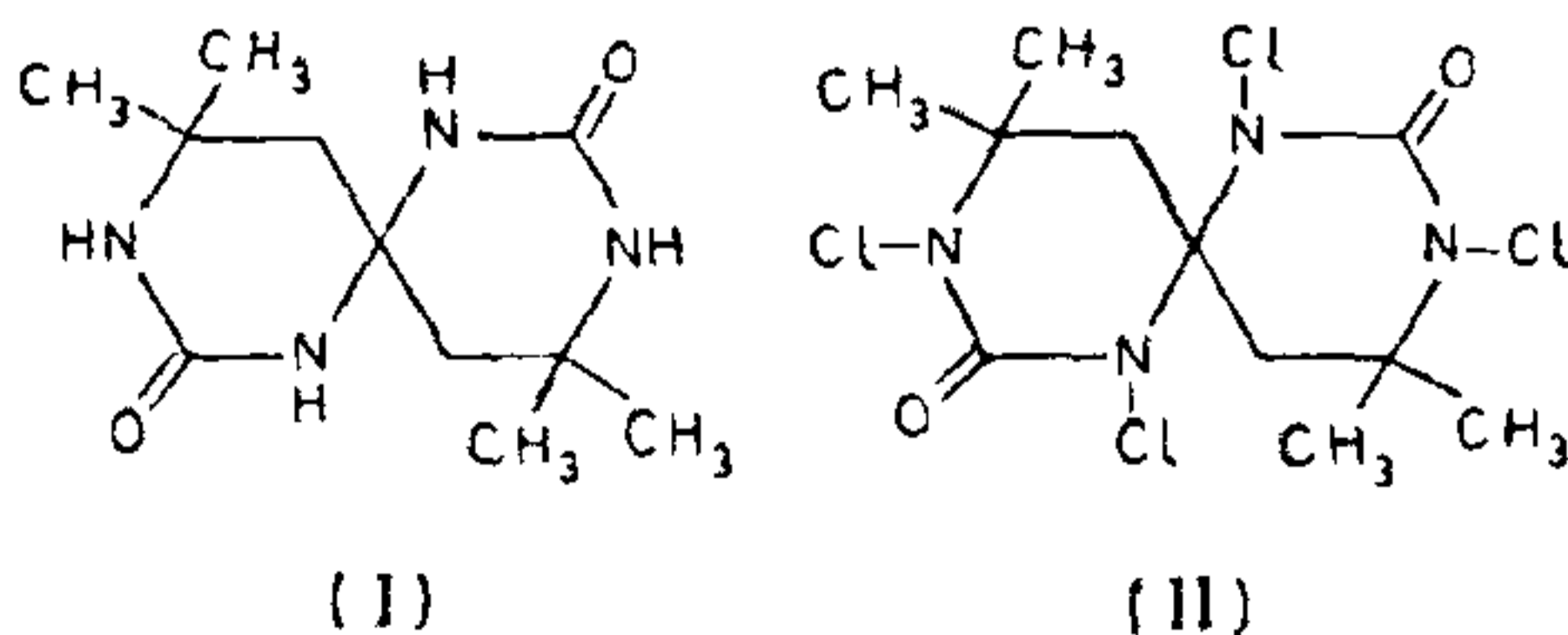
SYNTHESIS AND PHARMACOLOGICAL STUDIES OF 4, 4'-SPIRO-6, 6-DIMETHYL-TETRAHYDOPYRIMIDINE-2-ONE

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PYRIMIDINES are an integral part of the nucleic acid molecule. It is known that nucleic acids play a vital role in cellular functions and any alteration in structure is likely to produce mutagenic and other biological effects^{1,2}. Apart from nucleic acids, many other compounds (like antitumor drugs) contain pyrimidine or its derivatives^{3,4}. The present work describes the synthesis and some preliminary effects of 4,4'-spiro-6, 6-dimethyl-tetrahydropyrimidine-2-one on some haematological parameters and growth of the frog, *Rana tigerina*.

Urea (0.25 M) was dissolved in concentrated sulphuric acid (25 ml) and anhydrous acetone (0.75 M) was added in the course of 15 min at 15–20°C. The mixture was kept at this temperature for 48 hr. A white crystalline product which separated out was collected and washed with ice-cold acetone (2 × 25 ml). The crystalline product 4,4'-spiro-6, 6-dimethyl-tetrahydropyrimidine-2-one (I) was obtained (24.6 g, yield 82%) which was recrystallised from water, m.p. 266°C. (lit. 265°)⁵; γ_{\max} 3500, 3345 and 3210 (NH) and 1665 cm⁻¹ (C=O); n.m.r. spectrum (D₂O, δ); 2.10 (4H, s, 2CH₂) and 1.26 (12H, d, 4CH₃). The hydrogens of the NH groups have been exchanged with deuterium. Molecular weight (mass spectrometry) M. 240.2 C₁₁H₂₀N₄O₂ required M, 240.2.



N-chloro derivative of (I) was prepared by passing chlorine through an alkaline solution of (I) at pH9. A white crystalline N-chloro derivative (II) was obtained

(14.1 g; Yield 75%); m.p. 115°C (decom). γ_{\max} 1640 cm⁻¹ (C=O). Molecular weight (mass spectrometry) M, 378.0; C₁₁H₁₆N₄O₂Cl₄ required M, 378.0. It was difficult to take n.m.r of (II) because it was insoluble in almost all the solvents. The present study pertains to compound (I) only.

The frogs *Rana tigerina* weighing 60g were acclimatized in the laboratory for 10 days before use and were maintained at 30 ± 2°C during the study. 4,4'-spiro-6, 6-dimethyltetrahydropyrimidine-2-one (I) was dissolved in frog's Ringer at 60°C, cooled and injected in the ventral lymph sac of the animals at the rate of 50 mg/kg body weight. The controls were injected with the Ringer solution only, in the same way. Blood was collected at weekly intervals from five frogs each of control and experimental groups. The blood was immediately processed for haematology by employing the usual techniques. In the second experiment the weight changes of frogs treated with compound (I) were monitored for 10 days.

Mean values of the blood cells along with standard deviation have been given in figure 1. It is evident that compound (I) evoked a notable haematopoietic response. After one week, RBCs registered an increase of 5.42% over the control values, while the comparable values for the leukocytes and thrombocytes were 52.14 and 74.32% higher than the controls. The compound (I) elicited maximum effect on thrombocytes whereas leukocytes and erythrocytes followed this response (figure 1). The maximum values for both erythrocytes and thrombocytes were recorded after 3 weeks and thereafter the values showed a decline. The leukocytes on the other hand showed maximum values after two weeks and then started declining but at the end of 4 weeks, the values were still higher than those in the first week.

In the second experiment, only weights of the frogs were monitored. It was noticed that at a dose of 50 mg/kg of compound (I), the animals with initial low weight gained more weight as compared to those with initial higher weights.

These weight changes were statistically significant. Marked rise in the peripheral blood cell counts indicates that this new pyrimidine derivative (I) has initiated haematopoiesis or increased the release of cells from this system. Evidence is available that another pyrimidine derivative "Bromouracil" when fed to anaemic rats increased the synthesis of haemog-

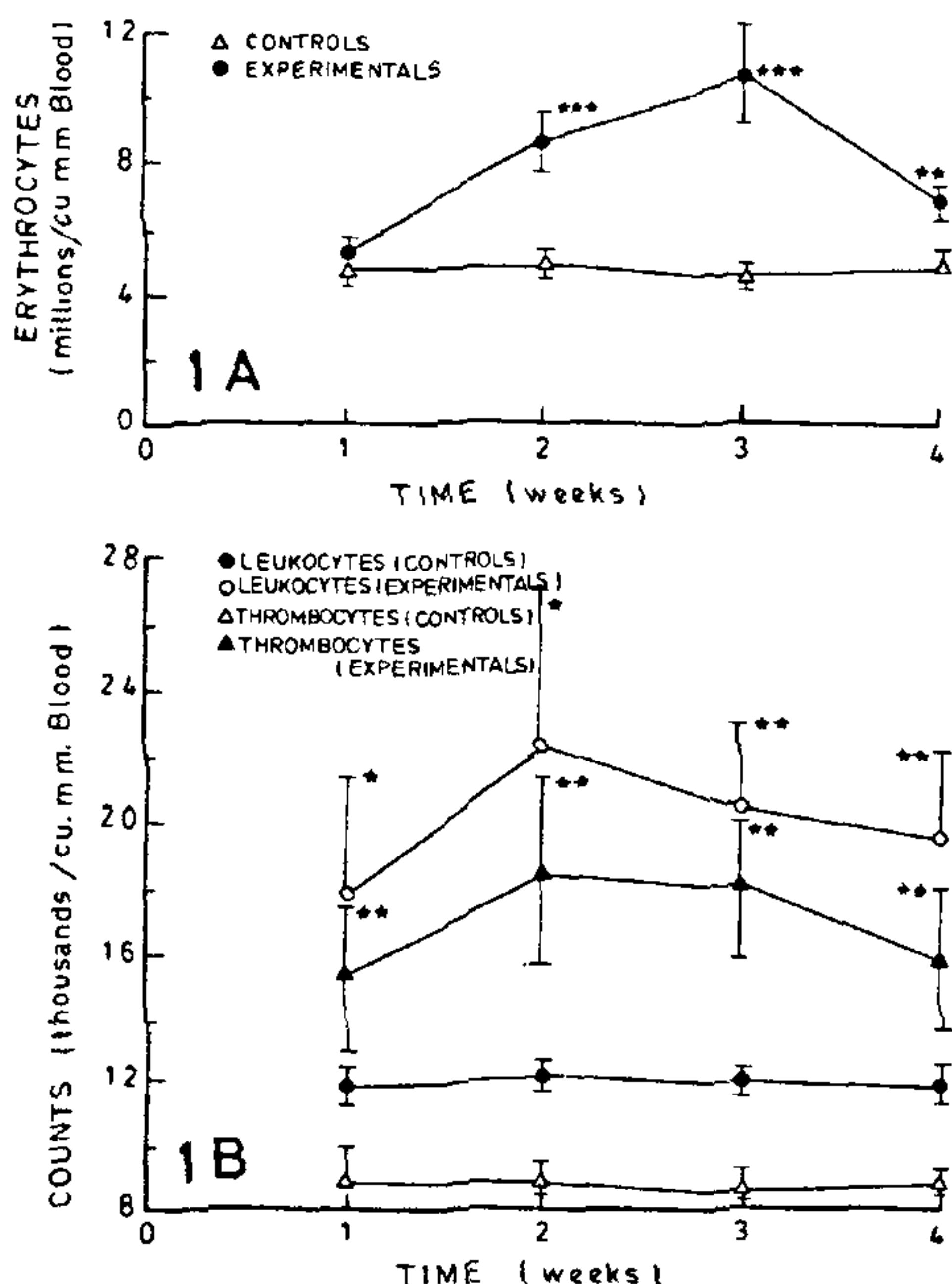


Figure 1. Effect of 4,4'-sprio-6, 6-dimethyltetrahydropyrimidine-2-one (50 mg/kg) on haematology of frog. A = Effect on erythrocytes. B = Effect on leukocytes and thrombocytes. Values with asterisks are statistically (*t* test) different from controls. * = $P < 0.05$; ** = $P < 0.01$; *** = $P < 0.001$

lobin and induced marked macrocythemia indicating early denucleation⁶.

The compound (I) also produced an increase in weight of frogs. Whether this increase is due to water imbibition or increased protein or fat deposition is not clear from the present study. Detailed studies on the pharmacological effects on intermediary metabolism in rabbits are in progress.

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1. Wang, S. W., *Fed. Proc.*, 1965, 24, S-71.
2. Schneller, S. W., Hosmane, R. S., Cartney, L. B., Mac. and Hassinger, D. A., *J. Med. Chem.*, 1978, 21, 990.
3. Tetsuo, T., Yosuke, N., Setsuro, F. and Tetsukiko, S., *Gan to Kagaku Ryoho (Jpn)*, 1978, 5, 1167.
4. Setsuro, F., Norio, U. and Setsuo, T., *Jpn Patent*,

1977, 77/39, 341, 05, *German Patent*, 1978, 2, 814, 202.

5. Butler, A. R. and Hussain, I., *J. Chem. Soc.*, (Perkin-II), 1980, 232.
6. Morio, S., *Acta Med. Okayama*, 1968, 22, 251.

RECENT FORAMINIFERA FROM OKHA BEACH SAND, GUJARAT STATE—A PRELIMINARY NOTE

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AMONGST marine micro-organisms, the foraminifera are excellent indicators of recent and geologically past environments. The ecology of the recent foraminifera has been studied in detail almost all over the world but it is still in a developing stage in this country. With the discovery of oil and gas in the off-shore Cenozoic strata of the country, the importance of recent foraminifera has increased; for not only do they provide precise age of these rocks but also help in the interpretation of their depositional environment. Hence, the current emphasis on the study of recent foraminifera in India is understandable.

The recent foraminifera of Indian coasts have been the concern of the Department of Geology, Aligarh Muslim University, Aligarh, for the last more than a decade. Under this research programme, several beaches of the east as well as west coast of India have been covered. The present paper deals with the preliminary results obtained from a study of recent foraminifera from the Okha beach sands, Western India, which, for the first time, deals with these micro-organisms from this area. The detailed investigation is in progress and will be published in due course.

Okha ($69^{\circ}04'35''$: $22^{\circ}28'30''$) is an intermediate port facing the Arabian Sea, in the State of Gujarat and has a long historical background. Samples of Okha beach sands were collected in February, 1984, for an extensive study concerning the taxonomy and ecology of recent foraminifera present therein.

As stated elsewhere, extensive work on the recent foraminifera has not been done in India. From the west coast, Kurian^{1,2} was probably the first to study the recent foraminifera and was followed by several workers³⁻¹².

During the course of the present investigation, a