ANTICOAGULANT ACTIVITY OF *HERACLENIN*

By

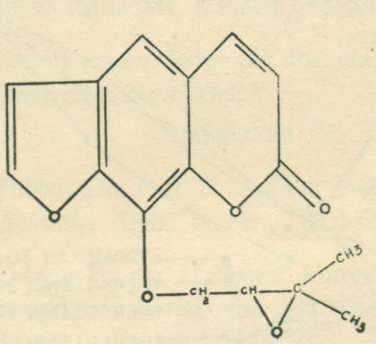
K.C MISHRA, R.C. SHARMA, Y.N. SHARMA AND R.B ARORA

Department of Pharmacology,
All India Institute of Medical Sciences, New Delhi

Heraclenin (4) is a new furocoumarin isolated from an Indian Medicinal Plant, Heracleum candicans (Umbelliferae) alongwith Heraclenol (5) and other furocoumarins. Its structure has been established as 8—(β, γ-oxido isoamyloxy)-psoralen. In view that Heraclenin was a coumarin derivative, it was proposed to investigate it for its anti-coagulant activity

CHEMISTRY

Heraclenin is a coumarin derivative having a furan ring attached to the carbon atoms 6 and 7 and β, γ-oxido isoamyloxy side chain on position 8 of the coumarin nucleus.



HERACLENIN

MATERIALS AND METHODS

The anticoagulant activity of Heraclenin was evaluated in male rabbits by determining the prothrombin time and coagulation valency (3, 1) and plasma clotting time (2) and compared with tromexan (ethyl biscoumacetate), after single oral doses of 30 *mg/kg*, 60 *mg/kg* and 120 *mg/kg*, of Heraclenin and 50 *mg/kg*, of tromexan. The results obtained are summarized in the Table.

Heraclenin was also chronically administered in a group of 4 rabbits for a period of 10 days.

RESULTS

The peak hypoprothrombinemic effect of Heraclenin after a single oral dose was achieved within 24—48 hours after a lag of 12—18 hours and the effect persisted for 4 to 5 days. The coagulation valency attained at the peak hypoprothrombinemic respons was 50, 54 and

TABLE I

Comparison of Anticoagulant Activity of Heraclenin and Tromexan

Property	*No. of expts.*	*Heraclenin 120 mg/kg*	*Tromexan 50 mg/kg*
1. Hypoprothrombinemic activity;	12		
(*i*) Onset of action		12 hours	24 hours
(*ii*) Peak action		24 hours	48 hours
(*iii*) Coagulation Valency at peak action		50%	50%
(*iv*) Duration of action;		120 hours	120 hours
2. Plasma clotting time		+35%	

60 percent after 120 *mg/kg*, 60 *mg/kg* and 30 *mg/kg*, doses of the drug, respectively. Coagulation valency of 50% was obtained at peak hypoprothrombinemic response, 48 hours after 5 *mg/kg*. of tormexan, and the effect lasted for 5 days (*Fig.* 1).

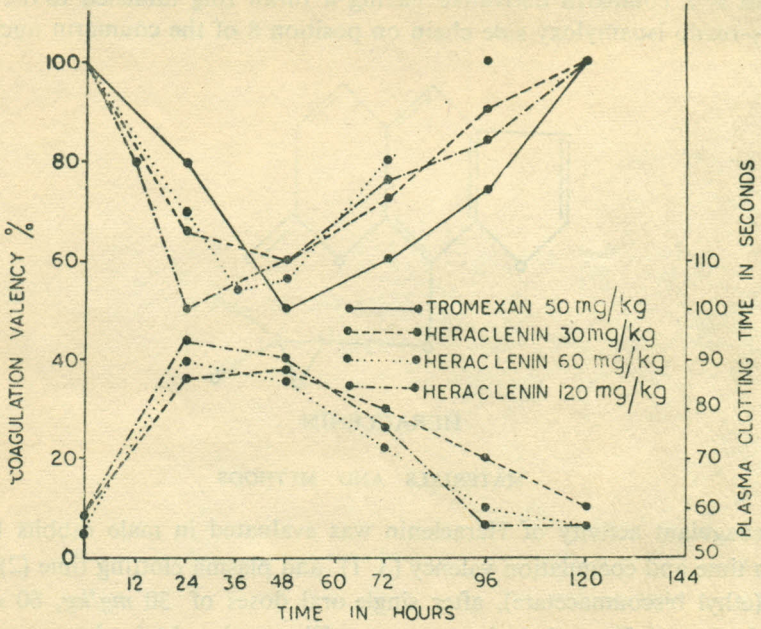


Fig. 1

The plasma clotting time increased by 30—35% after Heraclenin. Heraclenin was chronically administered to rabbits for a period of 10 days. The initial dose of 120 *mg/kg* brought down the coagulation valency between 50—55 percent after 36 hours. Subsequent doses of 60 *mg/kg*. every day maintained the coagulation valency between 50—60 percent. These rabbits were then sacrificed, macroscopic and microscopic examination of spleen, kidney, liver and mucous membranes revealed no evidence of haemorrhage.

DISCUSSION

Heraclenin possesses a significant anticoagulant activity in rabbits. It is evident from the results that the onset hypoprothrombinemia and peak effect was achieved earlier with Heraclenin than with tromexan. The duration of action is almost same for the two drugs.

The use of Heraclenin, therefore, permits a relatively rapid onset and a gradual recovery of hypoprothrombinemia with less likelihood of rapid fluctuations of prothrombin time. After prolonged administration of effective oral doses of Heraclenin to rabbits, no histological changes were seen.

SUMMARY

Anticoagulant activity of Heraclenin, an indigenous furocoumarin, was studied in male rabbits, by determining the Quick's time and plasma clotting time. It possesses significant anticoagulant activity, thus can find a suitable place in anticoagulant therapy.

The pharmacodynamic properties of Heraclenin are in progress.

ACKNOWLEDGEMENTS

1. The authors wish to thank Mr. S.P.S. Chauhan for his valuable technical assistance.

2. The authors gratefully acknowledge the financial assistance from Council of Scientific & Industrial Research, New Delhi.

REFERENCES

1. Montigel, C., and R. Pulver. Die Bestimmung der Prothrombinzeit mit der Thrombokinase 'Geigy' (G 23787). *Schweiz. Med. Wschr.*, **82**:132—135, 1952.

2. Owen, C.A. (Jr.)., D. Mann Frank, M. Hurn Margaret and J.M. Stickney. Evaluation of disorders of blood coagulation in the clinical laboratory. *Amer. J. Clin. Path.*, **25**:1417, 1955.

3. Quick, A.J., M. Stanley-Brown and F. Bancroft. A study of the coagulation defect in hemophilia and in jaundice. *Amer. J. Med. Sci.*, **190**:501, 1935.

4. Sharma, Y.N., A. Zaman and A.R. Kidwai. Chemical examination of Heracleum candicans—I. *Tetrahedron.*, **20**:87, 1964.

5. Sharma, Y.N., R.C. Sharma, A. Zaman and A.R. Kidwai. Chemical examination of Heracleum candicans-II. *Naturwisseschaften.*, **51**:537, 1964.