SHORT COMMUNICATION:

LOCAL ANAESTHETIC ACTIVITY OF SOME SEC-AMINO-N-(ARYL-ARALKYL)-ETHYL ACETAMIDES

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Summary: Six basic amides were screened for local anaesthetic activity and compared with procaine and lignocaine. Amongst the basic amides screened, piperidino-N-(α-4-ethoxy phenyl- β-phenyl) ethyl and Diethylamino-N (α-4-ethoxy- β-phenyl) ethyl acetamide were found to be more effective as compared to lignocaine. They were found to be non-irritant, and non-toxic even in high doses.

Key words: basic amides local anaesthetic activity

INTRODUCTION

Dalal and Trivedi (3) synthesized a series of lignocaine analogues in order to find more effective all purpose local anaesthetic compounds. Some of these compounds were tested by Patel and Jindal (5) and found to have more potent activity than lignocaine and other reference drugs. These findings have initiated trial of some more variants in basic structure. Patel and Trivedi (6) synthesized sec-amino-N-(aryl-aralkyl)-ethyl acetamides; some of these compounds were selected for testing local anaesthetic activity, irritation and toxicity.

MATERIALS AND METHODS

Six compounds were selected for study, and their chemical structures are shown in Table I.

Local anaesthetic activity:

The compounds were tested for intradermal anaesthesia on guinea-pig back by the method of Bulbring and Wajda(1) and surface anaesthesia on rabbit cornea by the method of Chance and Lobstein (2).

Local irritation:

Local irritation was determined in rabbits as described by Sharma (7) by the following tests.

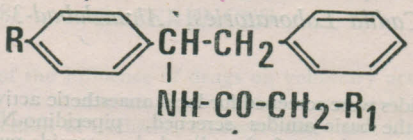
(1) Mucous membrane irriation by the rabbit eye test.

(2) Intradermal irritation by the trypan-blue test in rabbits.

Acute toxicity:

Mice (18 to 25 g) were given graded doses of the test compounds intraperitoneally. The animals were kept under observation for a period of 24 hrs. LD_{50} was determined according to the method of Karber (4).

TABLE - I Sec. Amino-N(aryl/aralkyl) ethyl acetamides.



Compound No.	R	R_1
1	OCH_3	Piperidino
2	OC_2H_5	"
3	OCH_3	Morpholino
4	OC_2H_5	"
5	OCH_3	Di-ethylamino
6	OC_2H_5	"

RESULTS

Local anaesthesia:

Surface anaesthesia: All the compounds studied showed surface anaesthetic properties generally in proportion to the concentration employed. Compounds 2,5 and 6 were ten times and compounds 1 and 4 were about twice as potent as lignocaine. Compound 3 was equipotent. The duration of anaesthesia was less as compared to lignocaine.

Intradermal anaesthesia: Graded concentrations ranging from 0.0125 to 0.4% of the compounds were injected intradermally. The compounds showed uniform relationship between anaesthetic effect and concentration. It is evident from the results (Table II) that the compounds 5 and 6 were ten times, compound 2 was six times and compounds 1,3 and 4 were approximately 1.5 to 2 times more potent than lignocaine.

Compounds 1, 3 and 4 were equipotent with procaine. Compounds 2,5 and 6 were four, seven and seven times more potent than procaine respectively.

TABLE II: Surface and intradermal tests for local anaesthetic activity of some basic amides.

Compound	*%concentration showing 50% local anaes±hetic activity ED_{50} ±SE*		*%concentration showing 100% or nearly 100% local anaesthetic activity*		*Duration at 100% activity min + SE*		*ID_{50} mg/kg ip in mice*
	Surface	*Intradermal*	*Surfae*	*Intradermal*	*Surface*	*Intradermal*	
1	0.04 ±0.007	0.045 ±0.008	0.1	0.1	8.0(0.4)	36.0(2.3)	290±10.2
2	0.0075±0.001	0.0125±0.003	0.025	0.05	10.3(0.3)	43.2(2.6)	340±12.1
3	0.075 ±0.012	0.05 ±0.008	0.2	0.2	8.1(0.9)	36.1(2.0)	350±12.6
4	0.03 ±0.006	0.04 ±0.007	0.2	0.2	9.4(0.9)	41.8(4.1)	289± 9.8
5	0.0075±0.001	0.0075±0.001	0.05	0.05	10.6(3.1)	44.1(3.4)	220± 7.8
6	0.0075±0.0012	0.0075±0.001	0.025	0.025	8.36(0.9)	42.1(2.6)	197± 8.2
Lignocaine	0.075 ±0.01	0.075 ±0.013	0.2	0.2	15.0(0.8)	54.1(4.6)	—
Procaine	—	0.05 ±0.01	—	0.4	—	57.0(. .2)	—

Irritation test:

None of the compounds showed any irritation upto 0.4% concentration.

Acute toxicity:

None of the compounds showed depressant action on the central nervous system. The LD_{50} (*mg/kg*) was 290,340,350,289,220 and 197 for the compounds 1,2,3,4,5 and 6 respectively.

DISCUSSION

Amongst the compounds studied, compounds 5 and 6 were about ten times as potent as lignocaine for both surface and intradermal anaesthesia, and were the most potent among the series.

Compounds 5 and 6 have a diethylamino at R_1. Compound 5 has methoxy and 6 has ethoxy group at R position. Compound 6 was found to be the most potent.

Substituting piperidino at R_1 gives compounds with intermediate activity. Substituting morpholino at R_1 gives compounds having less activity.

The duration of anaesthesia with compounds 6 and 5 was sufficiently long and was proportional to the concentration employed. All the compounds were free from irritation and toxicity.

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