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# Effect of cathinone on chick embryo heart*

C. K. MAITAI, *Department of Pharmacy, University of Nairobi P.O. Box 30197, Nairobi, Kenya*

The pharmacological profiles of indirectly acting sympathomimetic amines are qualitatively similar and they also show structural similarity. Ephedrine, a prototype for the group, has been shown to exhibit a biphasic response on isolated mammalian heart; at low concentration, it enhances contractility while at higher concentrations it causes negative inotropic activity which can be blocked by atropine (Goldberg & Shideman 1967). Cathinone a potent central nervous system stimulant, recently isolated from the plant *Catha edulis* is a phenylalkylamine and preliminary studies indicated that its pharmacology closely resembles that of sympathomimetic amines in some respects (United Nations Narcotic Laboratory document MNAR/3/79 GE 79-10365).

In the present report the response of chick embryo heart (CEH) to cathinone is described and evidence is presented that the cardiodepressant actions on both inotropic and chronotropic responses are not mediated through release of acetylcholine. The main advantage of CEH over the classical Langendorff mammalian heart preparation is that it is small (2–4 mg), easily oxygenated and a large proportion of its receptors are accessible to the drug molecules.

Fertile eggs from Babcock hens were maintained at 37 °C and approximately 85% humidity in a Humaidare incubator (Humaidaire Incubator Co Wayne at New Madison, Ohio, USA). After 7 days of incubation, the embryos were removed from eggs and placed in Tyrode solution of the following composition (mM): NaCl, 12; KCl, 4·77; $CaCl_2$, 2·38; $KHPO_4$, 0·6; $MgSO_4$, 0·6; $NaHCO_3$, 25 and glucose 5. The excised hearts were set up as described by Lelorier & Shideman (1976) in a 15 ml tissue bath containing Tyrode solution, warmed to 33–34 °C and gased with 5% $CO_2$ in oxygen. In some experiments, the eggs were incubated for 5 days. The heart was allowed to equilibrate for 40 min to allow the heart rate and contractility to stabilize. Drugs solutions were then added to the bath and the effect recorded for 7 min using a linearsyn Variable differential transformer (Hewlett-Packard Co, Palo Alto, California, USA) the signal from which was recorded on a Gilson M5P Minipolygraph fitted with an LVDT amplification channel (Gilson Medical electronics, Middleton, Wis USA). In all cases washing of the tissue was by a simple overflow technique using 150 ml warmed oxygenated Tyrode solution per wash.

In the preliminary experiments it was shown that acetylcholine ($10^{-6}$ mM) had negative chronotropic and inotropic effects while adrenaline ($10^{-6}$ mM) had positive inotropic and chronotropic effects on CEH preparations. Atropine in concentrations of up to $10^{-3}$ mM had no significant effect on CEH. The effect of cathinone on CEH (Table 1) indicated that it had a cardiodepressant action on both 7 day and 5 day CEH which was not blocked by atropine. Furthermore, since the 5 day CEH is not cholinergically innervated (Romanoff 1960) it is reasonable to conclude that the cardiodepressant effect is not mediated through the release of acetylcholine.

Table 1. Effect of cathinone and ephedrine on chick embryo heart.

| 7 day heart | | Changes* (% of control) Heart rate mean ± s.e. (n = 3) | Contractility mean ± s.e. |
|---|---|---|---|
| Drug (concn mM) | | | |
| Cathinone | $1 \times 10^{-4}$ | 0 | −3·6 ± 1·2 |
| | $2 \times 10^{-4}$ | 0 | −6·6 ± 1·5 |
| | $4 \times 10^{-4}$ | −8·5 ± 2·5 | −12·3 ± 0·1 |
| | $1 \times 10^{-3}$ | −18·2 ± 4·1 | −15·9 ± 1·6 |
| | $2 \times 10^{-3}$ | −17·2 ± 1·9 | −25·7 ± 1·7 |
| | $4 \times 10^{-3}$ | Heart stopped for 20 s | |
| Cathinone and atropine | $1 \times 10^{-3}$ / $4 \times 10^{-3}$ | −17·6 ± 2·4 | −14·6 ± 1·8 |
| Ephedrine | $1 \times 10^{-4}$ | 0 | +22 ± 4 |
| | $2 \times 10^{-4}$ | 0 | +5 ± 3·2 |
| | $4 \times 10^{-4}$ | −10·4 ± 1·8 | −14 ± 1·6 |
| | $5 \times 10^{-4}$ | −12·5 ± 2·5 | −16 ± 2·4 |
| Ephedrine and atropine | $5 \times 10^{-4}$ / $4 \times 10^{-3}$ | −1·2 ± 0·8 | −2·0 ± 1·6 |
| Atropine | $4 \times 10^{-3}$ | 0 | 0 |
| 5 day heart | | | |
| Cathinone | $1 \times 10^{-4}$ | −1·7 ± 1·7 | −2·7 ± 1·6 |
| | $2 \times 10^{-4}$ | −16·8 ± 1·4 | −20·4 ± 1·8 |
| | $4 \times 10^{-4}$ | −40·5 ± 2·2 | −26·2 ± 2·7 |
| | $5 \times 10^{-3}$ | −52·1 ± 5·2 | −72·3 ± 3·3 |
| Ephedrine gave weak inconsistent results. | | | |

* Minus sign denotes decrease, plus sign denotes increase; n = number of experiments performed on different CEH preparations.

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