

CARDIAC AND INTESTINAL CONTRACTIONS UNDER THE INFLUENCE OF TRITURATED DRUG DILUTIONS

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ABSTRACT

Triturated dilutions of acetylcholine and adrenaline are found to produce reverse effects than their parent one on the mechanical performance of mammalian heart and intestine in vitro. However, there is a variation in the magnitude of reverse response observed for both the tissues. It is concluded that variation in the effect of triturated dilutions is probably due to handling and shaking of the diluted drug before use in experiments. In addition, no relation exists between degree of dilution and the magnitude of response for both the tissues.

INTRODUCTION

Mammalian heart and intestine have long been used as a tool for various pharmacological and physiological studies. In these studies effects of various drugs dilutions have been reported on mammalian perfused heart (Boyd, 1968). Similarly, triturated drug dilutions have also been used to study their effects on intestinal activity (Arita et al., 1997). Dilutions of acetylcholine of 10^{-7} demonstrated responses in isolated small intestine of Guinea Pig and Rabbit (Guggenheim & Loftier, 1916b; Fuhner, 1916; Kendall and Shumate, 1930).

However, Boyd (1968) was the first scientist who reported reverse effect of various drug dilutions on tissues. After this study, reports are not available regarding the effects of drug dilutions on tissues in vitro or in vivo. Recently, Arifa, et al. (1995) investigated the effects of simple and triturated dilution (10^{-3}) on intestinal activity. Moreover, Erum, et al. (1997) reported the effects of simple and triturated dilution of Acetylcholine on cardiac activity. In both of these studies reports on intestinal and cardiac activity, triturated dilutions of acetylcholine were found to exhibit reverse effects at 10^{-3} dilution.

It has been described in homeopathy that dilution of drug by succession and trituration produce a change in the original molecule of drug. This change has been indicated (Arita, et al., 1997) to be responsible for the reverse effect than its original concentrated one.

The object of the present study was to find out the effects of a wide range of triturated dilution of Acetylcholine and Adrenaline (from 10^{-3} to 10^{-12}) on both the intestinal and cardiac contraction parameters for the investigation of reverse effects.

MATERIALS AND METHODS

Trituration:

Triturated drug dilutions were prepared by using the concentrated drug which was serially diluted as 1:1. This dilution was triturated for 2hrs by using a mechanical shaker. After trituration, one part of this dilution was further diluted with 10 parts of deionized water. This new dilution was again triturated for 2 hrs. Later, this dilution was further diluted with 10 parts of deionized water. This new dilution was again triturated for 2 hrs. Later, this procedure was continued till the higher dilution required was obtained.

Animals:

Both the sexes of Rabbit *Oryctolagus cuniculus* were used weighing 1.5 to 2 Kg.

Studies on Cardiac Performance:

The animal was sacrificed and chest was opened to isolate the heart by carefully locating the aortas and other vessels including vena cava and pulmonary. The isolation was as quick and the heart was immediately transferred in 500ml chilled oxygenated Krebs solution for washing and closing the Vena Cavae and Pulmonary vessels. The heart was later firmly tied with heart cannula on perfusion assembly. This perfusion assembly has the ability to provide the perfusate at a constant temperature of 37.5°C for heart. The apex of the heart was then hooked with the isotonic transducer for mechanical recordings obtained on the oscillograph (Harvard Bioscience).

Studies on Intestinal Performance:

The animal was sacrificed and abdomen was opened to isolate the ileum by carefully locating the jejunum and ileocecal end. Later, a large piece of ileum was removed and kept in 1000ml of oxygenated Krebs's solution for washing and preparation of intestinal strips. The strips were of 2.5 to 3 cm in length that were mounted in the organ bath assembly having oxygenated Krebs's solution in its gut tube at 37.5°C. Rhythmic activity was then recorded using auxotonic transducer on minigraph (Lafayette).

Recordings and Measurements:

All mechanical recording obtained from heart and intestinal activity pre and post administration of drug dilutions in gut bath were used for the measurement and calculation of force and rate of cardiac and intestinal contractions.

RESULTS

Various parameters measured and calculated from mechanical recordings obtained from the perfused mammalian heart and isolated pieces of intestine demonstrated effects of triturated dilutions of acetylcholine and adrenaline ranging from 10⁻³ to 10⁻¹².

Effect of Triturated Dilution of Acetylcholine:

Triturated dilutions (10⁻¹² and 10⁻¹¹) of acetylcholine showed prominent and significant reverse effect on heart rate (Table I) along with 10⁻⁶ and 10⁻⁷, where both the cardiac force and heart rate showed reverse effect but were not significant (Table I).

Effect of Triturated Dilutions of Adrenaline:

The triturated dilutions of adrenaline demonstrated reverse effect at 10-5, 10-6 and 10-7 dilutions. This effect was prominent and significant for cardiac force while it was less and insignificant for heart rate (Table 2). Similarly, triturated dilutions of adrenaline showed reverse effect on intestinal force of contraction at 10-5, 10-6, 10-7, 10-8 and 10-12 dilutions. However, the intestinal rate of contraction was found to demonstrate reverse effect of Adrenaline at 10-5, 10-9, 10-10 10- 11 dilutions.

DISCUSSION

According to the results obtained by using the triturated Acetylcholine and adrenaline dilutions on the cardiac activity, it is clear that various dilutions showed their reverse effect on both the force and rate of cardiac contraction (Fig 1). However, this reverse effect of acetylcholine was less pronounced on cardiac force parameter as shown in Table I and 2 for 10-6 10-7 than the reverse effect of adrenaline on this parameter at 10-5, 10-6, and 10-7. However, 10-6 < 10-9 < 10-10 < 10-12 < 10-11 dilution of acetylcholine produced prominent and significant reverse effect in the above order on rate of cardiac contractions. It is however, to be noted that 10-3 dilution of adrenaline did not produced reverse effect on cardiac force as reported earlier on intestinal force by this dilution (Arita et al., 1997). Further remaining dilution of both the acetylcholine and adrenaline other than stated above produced positive effect of both of these drugs on cardiac performance.

In our opinion, the variation in the magnitude of effect produced by different dilution probably reflects a variation in the change in drug molecule during trituration. It is also evident that there is no criteria that may be established to explain the relation between increase in dilution and in the response of cardiac force or rate, from the data collected. It is therefore a bizarre reverse effect obtained from cardiac performance under the influence of triturated acetylcholine and adrenaline dilution.

In the results obtained from experiments performed on intestinal contractions, the above mentioned bizarre effect was also evident. In these results the triturated acetylcholine dilutions of 10-5, 10-9, 10-10 and 10-11 demonstrated reverse effect (Fig. 2) on intestinal force while it was at 10-8, 10-10 and 10-11 on intestinal rate of contraction. Similarly, adrenaline dilutions demonstrated reverse effect at 10-5, 10-6, 10-7, 10-8 and 10-12 on intestinal force and at 10-5, 10-9, 10-10 and 10-11 on intestinal rate of contractions. The remaining dilution of adrenaline and acetylcholine did not produced reverse effect.

From the above discussion it is concluded that trituration results in some change in the original drug molecule that is able to produce a dissimilar effect than the original one. But this effect is not observed always in all experiments.

In our opinion, after trituration, the degree of shaking and handling of diluted drugs before administration may be held responsible for such variation in the tissue response.

It is further concluded that triturated drug can produce reverse effect irrespective of the type of tissue, i.e., cardiac or smooth muscle.

Table 1

Effect of triturated adrenaline dilutions on force and rate of cardiac and intestinal contraction parameters calculated as percent of their controls. These values were obtained from six experiments performed for the recording of both the cardiac and intestinal activities

Dilutions	Cardiac		Intestine	
	Force	Rate	Force	Rate
10-3	192.6	117.8	---	---
10-4	115.7	99.8	---	---
10-5	86.7	91.1	178.3	105.9
10-6	79.3	106	107.1	11.1
10-7	98.7	99.6	177.5	97.2
10-8	---	---	126.5	90.5
10-9	---	---	88.2	102.7
10-10	---	---	91.4	105.6
10-11	---	---	37.4	105.6
10-12	---	---	141.7	100

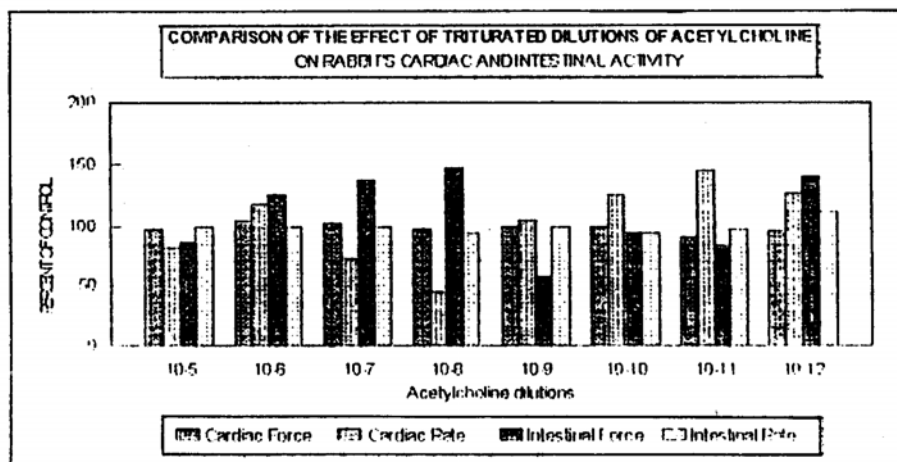
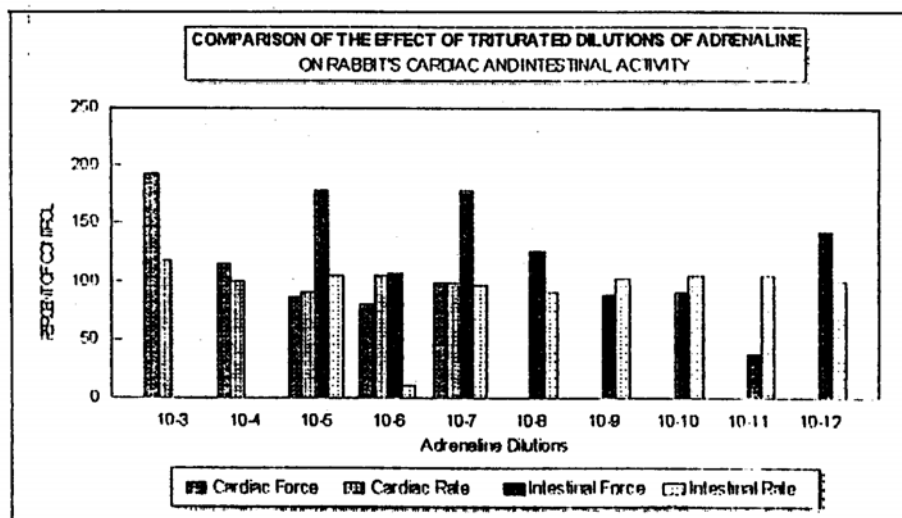


Table 2

Effect of triturated acetylcholine dilutions on force and rate of cardiac and Intestinal contraction parameters calculated as percent of their controls. These values were obtained from six experiments performed for the recording of both the cardiac and intestinal activities.

Dilutions	Cardiac		Intestine	
	Force	Rate	Force	Rate
10-3	---	---	---	---
10-4	---	---	128	101.5
10-5	96.8	81.5	87	100
10-6	102.8	117.8	125	100
10-7	101.4	72.8	137	100
10-8	96.8	45.7	147.7	94
10-9	100	104	58	100
10-10	100	125	94	94
10-11	91	144	82.5	97
10-12	96	126	140	111

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