EFFECT OF EXOGENOUS CALCIUM IONS ON PROSTAGLANDINS OUTPUT FROM RAT HEPATIC TISSUE SLICES

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Received for Publication: 3/4/1990

INTRODUCTION

The requirement of extra and/or intracellular CQ++ to stimulate prostaglandins synthesis varies in different tissues.

Poyser, (1985), elicited that prostaglandins synthesis and efflux from their active biosynthetic sites in almost tissues is dependent upon mobilization of Ca++ from intracellular stores. The extracellular Ca++ is essential for release of Ca++ from intracellular stores and essential for replenish these stores., Rilley & Poyser, (1987).

Ernest et al., (1983), reported that the activity of phospholipase seems to be increased by the presence of Ca++.
PLA2 is extremely important in the release of arachidonic acid, (which is the most abundant of prostaglandins precursors in almost all the tissues), followed by a rise of prostaglandins biosynthesis. So PLA2 is considered as a regulating and triggering enzyme for prostaglandins biosynthesis.

Prostaglandins are not stored pre-formed but are synthesized and released as required. Therefore the increased efflux reflects the increased biosynthesis and not release of prostaglandins as endogenous constituents Ramwell & Shaw, 1970 and Olley & Coceani, (1980).

Synthesis of PGF2 & may be derived from PGE2 and/or from PGD2. The interconversion between PGF2 & and PGF2 is dought, Yamamoto, (1983), reported that there is no a direct interconversion between PGE2 and PGF2 &. In contrast Ernest et al., (1983) found that reduction of the Ketogroup at C9 in PGE2 to form PGF2 & compound is found to take place in guinea pig as well as in human.

The aim of the present work is to study the effect of extracellular Ca++
is composed with that obtained by Olsen.

phosphate buffered solution. This data
caused PGE2 output from the hepatic issue
receptor, FGF 3, in Kek's Fringer
slices incubated in Krebs-Ringer
slices incubated in Krebs-Ringer

in this study the addition of calcium

discussion

If this will be illustrated in table 1.

Data: The hepatic issue slices to
put from the hepatic issue slices to
high significant increase in PGE2-2
a significant decrease in PGE2-2 with
ion (10 ng/ml) (26 pg/ml) (26 pg/ml) (26 pg/ml) (26 pg/ml)
addition of calcium gluconate solu-

results

was less than 0.05.

polysis was rejected when P value
paired Student's "t" test; the null hy-
M. The data were analyzed by un-
results are expressed as ± S.E.

statistical analysis:

Badre & Raveel Diagnostic Inc.

assay. The kits were supplied from
binding principles of Radio-immuno-
which depends on the competitive
coating to Yelow and person (1971).'

PGE2 and PGE2 α (concentration 2x)
which were used for determination of

material and methods

Effect of Exogenous Calcium Ions On EtC.

was removed and aliquots of the me-
for 2 hours at 37°C. The liver slices

assay

were added to the incubation media
media in a dose of 25 ng/ml wet tis-
Carcio, were added to the incubation
produced by Swiss Pharmaco S. A.
Calcium gluconate ampoules 10%

al. (1975).

The tissues were harvested throughly with-
sue slices were excised from the ani-
The rats were scalled. The liver is.

tissue preparation:

say vitamins and minerals.
with milk, bread, carrots and all nece-
study. The rats were feed at libitum
grams were used in this experiment.

made abino rats weighing 150-200

material and methods

Effect of abino rats.

prostaglandins metabolism in hepatic
side role of extracellular Ca++ on the

pathic issue slices to elucidate the poss-
on PGE2 and PGE2 α output from he-
et al., (1983), Poyser (1985) and Riley & Poyser (1987), they reported that prostaglandins output is stimulated by Ca++ ions. Prostaglandins synthesis and efflux from their active biosynthetic sites are dependent upon mobilization of Ca++ from intracellular stores with a direct interaction with the membranes of endoplasmic reticulum, the main site of PLA2 and prostaglandins synthesizing enzymes. The extracellular Ca++ releases the intracellular Ca++ from its stores, and is essential for replenishing these intracellular stores.

Weis & Malik (1985), elicited that activation of beta-adrenergic receptors will stimulate cardiac PGE2 and 6-keto-PGF1α synthesis. It is absolutely dependent on extracellular Ca++. Activation of these beta receptors increase transmembrane Ca++ influx, which by activating release of Ca++ from its intracellular stores, stimulate a release of arachidonic acid consequent to activation of phospholipase A2, making free arachidonic acid available for PGs synthesis.

Recently it has been reported that 6-keto PGF1α synthesis in the rat aortic rings elicited by norepinephrine was abolished completely by removal of Ca++ from the medium and by Ca++ channel blockers, verapamil and nifedipine. Stewart et al., (1984).

Cooper and Malik (1986), concluded that norepinephrine requires extracellular as well as intracellular Ca++ to express its maximal effect on renal PGs synthesis.

Ca++ that is released from intracellular sites interact with calmodulin. By a specific calmodulin antagonist, rendering calmodulin biologically inactive, basal and stimulated PGE2 efflux markedly inhibited. In addition calmodulin antagonists might also inhibit PGE2 efflux by interfering with Ca++-phospholipid sensitive protein kinase C. Activation of protein Kinase C might activate release of Ca++ from intracellular stores, thus inducing PGE2 output. Levis & Weiss, (1976) Picket et al., (1977) and Cooper, & Malik, (1986).

Broekemeier et al., (1985), showed that verapamil exerted a moderate degree of phospholipase A2 inhibitory activity, whereas the other calcium channel blockers, diltiazem and nifedipine, exhibited only weak inhibition of rat liver mitochondrial phospholipase A2 activity.

Recently Danon et al., (1986), reported that verapamil, at different concentrations, exerts a dual action on
The effect of Ca++ ions on prostaglandins formation as a result of increase or decrease in metabolism is under study the possible role of Ca++ ions in prostaglandins formation.

**SUMMARY AND CONCLUSION**

In detail in further investigation enzymes. This point must be studied on the activity of the second messenger Ca++ ions may have a role of Ca++. First, PGE-2 activity enzyme increases by Ca++. A through inhibition of Ca++ decreases the conversion of PGE2 to 6-keto-PGF1α and decreases the synthesis of PGE2. PGE2 via the synthesis of 6-keto-PGF1α decreased the conversion of PGE2 to PGE2 and decreased the synthesis of PGE2.

From the present study, it is concluded that addition of extracellular media resulted in a high increase in secretion of PGE2 with a significant decrease in PGE2 synthesis. This decrease can be attributed to one of the following:

1. Addition of calcium gluconate to the incubation media resulted in a high increase in secretion of PGE2 with a significant decrease in PGE2 synthesis. This decrease can be attributed to one of the following:
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Table (1): Effect of calcium gluconate on PGE2 and PGF2α output from isolated hepatic tissue incubated for 2 h. at 37°C.

<table>
<thead>
<tr>
<th>The tested group</th>
<th>PGE2 (ng/gm tissue)</th>
<th>PGF2α ng/gm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Control group mean</td>
<td>29.362</td>
<td>33.625</td>
</tr>
<tr>
<td>± S. E. M.</td>
<td>5.058</td>
<td>2.251</td>
</tr>
<tr>
<td>2. Calcium group Mean</td>
<td>47.451</td>
<td>14.504</td>
</tr>
<tr>
<td>± S. E. M.</td>
<td>4.341</td>
<td>2.413</td>
</tr>
<tr>
<td>P</td>
<td>0.05*</td>
<td>0.05*</td>
</tr>
</tbody>
</table>

* Highly significant.
REFERENCES


الملخص العربي
أجري هذا البحث لدراسة تأثير أيونات الكالسيوم على البروستا جلاندين المستخرج من خلايا كبد الفئران البيضاء.

وقد أدت نتائج البحث إلى أنه اضافة أيونات الكالسيوم إلى محلول كريس رينجر فرسانات المحضن للخلايا بجرعة 49 ميكروجرام لكل جرام من وزن الأنسجة على هيئة جلوكوات الكالسيوم قد ساعد على زيادة كمية البروستا جلاندين E2 المستخرج من خلايا الكبد زيادة ذات دلالة إحصائية عالية. كما أنه أدى إلى نقص كمية البروستا جلاندين المستخرج من خلايا الكبد وهذا النقص ذو دلالة إحصائية عالية مما يدل على أن أيونات الكالسيوم لها دور فعال في عملية تكوين البروستا جلاندينات وتحويل كل من النوعين E2 & F2 إلى الآخر.