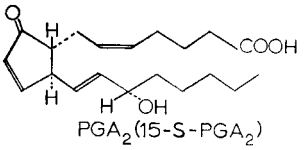
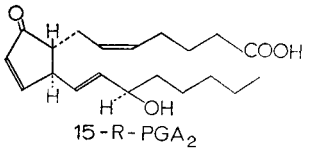
# Cardiovascular effect of a prostaglandin isolated from a gorgonian *Plexaura homomalla*

Recently, Weinheimer & Spraggins (1969) isolated a prostaglandin (PG) $A_2$-like compound (II) from a sea animal, gorgonian, *Plexaura homomalla*. They found that the Sf value in thin-layer chromatography and the infrared and nuclear magnetic resonance spectra of this compound are identical with those of $PGA_2$ (I). The present study was undertaken to compare the cardiovascular effects of this compound with those of $PGE_2$ and $PGA_2$ in anaesthetized dogs.




$PGA_2$(15-S-$PGA_2$)

I




15-R-$PGA_2$

II

Fifteen dogs weighing between 20 and 25 kg were anaesthetized by the intravenous administration of 30 mg/kg of sodium pentobarbitone. The technique to measure heart rate, systemic arterial pressure and myocardial contractile force were described previously (Nakano, 1967; Nakano & Kusakari, 1968). All haemodynamic parameters measured, except heart rate, were recorded simultaneously and continuously with an Electronics for Medicine recorder (DR8). $PGE_2$ and $PGA_2$ were obtained from Dr. J. Pike of the Upjohn Company, Kalamazoo, Michigan. The $PGA_2$-like compound was isolated from *Plexaura homomalla* and supplied from Dr. A. J. Weinheimer, Department of Chemistry, University of Oklahoma, Norman, Oklahoma. The purity of each PG compound was ascertained by thin-layer chromatography using the solvent systems described by Green & Samuelsson (1964).

The results of the cardiovascular effects of $PGE_2$, $PGA_2$ and $PGA_2$-like compound from the gorgonian are summarized in Fig. 1. The haemodynamic effects of both $PGE_2$ and $PGA_2$ were qualitatively similar to those of $PGE_1$ and $PGA_1$ (Nakano & McCurdy, 1967, 1968). The intravenous administration of 0·25–4·0 $\mu$g/kg of $PGE_2$ and $PGA_2$ increased heart rate and myocardial contractile force as mean systemic arterial pressure decreased. The haemodynamic changes induced by both $PGE_2$ and $PGA_2$ were essentially in proportion to the dose. In contrast, the intravenous administration of 2·25–256 $\mu$g/kg of the $PGA_2$-like compound isolated from the gorgonian caused no essential change in the three haemodynamic parameters.

Subsequently, further chemical and spectral analysis of this compound in the laboratory of Dr. A. J. Weinheimer showed it to be a 15-epimer of $PGA_2$ (15-*S*-$PGA_2$), 15-*R*-$PGA_2$ (II). According to the sequence rules formulated by Cahn, Ingold & Prelogg (1956), the priority sequence at the asymmetrical C-15 in this compound is directed in the *R* configuration instead of being *S* as with $PGA_2$. The sterochemical modification at C-15 in $PGA_2$ abolished completely its cardiovascular effects in dogs, although this structure activity relation observed in this present study is not a unique phenomenon in pharmacodynamic action of drugs. The gorgonian was

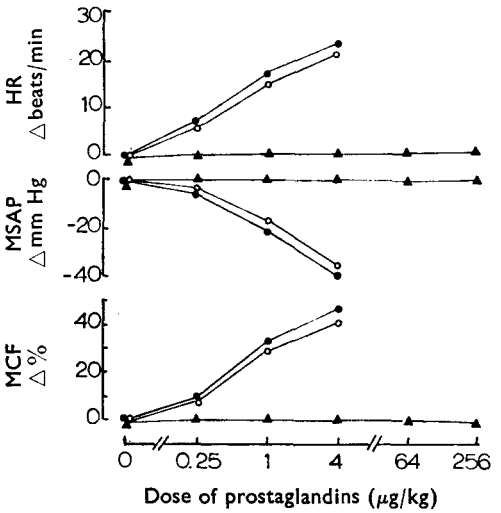



FIG. 1. Effects of the i.v. administration of graded doses (0·25–256 μg/kg) of $PGE_2$, $PGA_2$ and 15-*R*-$PGA_2$ on heart rate (HR), mean systemic arterial pressure (MSAP) and myocardial contractile force (MCF) in 15 dogs. Each value represents the mean of the maximal effects caused by each prostaglandin. ● $PGE_2$; ○ $PGA_2$; ▲ 15-*R*-$PGA_2$.

found to contain high concentrations of 15-*R*-$PGA_2$, amounting to 0·01–0·1% of its dry weight. Although this compound has no cardiovascular effects in dogs, it is tempting to speculate that 15-*R*-$PGA_2$ may play important physiological and biochemical roles. Further studies are indicated to elucidate this problem.

The author is indebted to Dr. J. E. Pike of the Upjohn Company, Kalamazoo, Michigan, and to Dr. A. J. Weinheimer for the generous supplies of $PGE_2$, $PGA_2$ and 15-*R*-$PGA_2$.

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