Applications of liquid-gel partition chromatography in the prostaglandin field

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Lipophilic-hydrophobic dextran gels can be used for the straight-phase or reversed-phase separations of lipids (Ellingboe, Nyström & Sjövall, 1970). Among the advantages of these systems are high resolving power, high loading capacity, quantitative recovery of submicrogram amounts of material and reusability of the columns. Column chromatography systems have been described for the reversed-phase separation of E and F-type prostaglandins (Nyström & Sjövall, 1973) and the straight-phase separation of a wide variety of prostaglandin methyl esters (Brash & Jones, 1974). We will demonstrate the principles of the method, the factors influencing the choice of a gel and solvent system for a particular purpose and the applicability of the chromatography systems to the following areas of the prostaglandin field.

(a) Purification of 15(S) and 15(R) prostaglandin epimers

The synthesis of novel prostaglandins often involves the production of the 15(S) and 15(R) epimers. The biological properties of these isomers is usually considerably different and complete separation is desirable. The resolution of a number of pairs of epimers with widely different substituents in the cyclopentane ring has been achieved using straight-phase gel systems. The separation of 15(S) and 15(R) PGA_2 methyl esters derived from an extract of the coral *Plexaura homoalla* will be shown.

(b) Separation and purification of PGE_2 metabolites from liver homogenates

It has been shown that rabbit liver homogenates convert PGE_2 into $PGF_{2\alpha}$ and several less polar metabolites (C.N. Hensby, unpublished results), all of which can be separated on a straight-phase gel system. Using a single column many samples may be processed consecutively, and the elution volumes of individual compounds are highly reproducible. Should the column become contaminated with polar material, it may be purged by reversed flow with a more polar eluant and then re-equilibrated with the normal eluant.

(c) Separation and purification of $PGF_{2\alpha}$ urinary metabolites from the rat

These compounds are considerably more polar than $PGF_{2\alpha}$ mainly due to β-oxidation of the α-side chain to give ^{18}C and ^{16}C metabolites, and ω-oxidation to give dioic acids. The reversed-phase systems described by Nyström and Sjövall (1973) have been used to completely resolve most of these compounds as their methyl esters. One major metabolite of subcutaneously administered $PGF_{2\alpha}$ has been identified as 5α,7α-dihydroxy-11-oxo-prosta-1,14-dioic acid in which β-oxidation of both side chains has occurred. The methyl ester of this compound on straight-phase gel chromatography appears to be excluded from the gel and is eluted with material less polar than $PGF_{2\alpha}$ methyl ester. The elution profiles of several $PGF_{2\alpha}$ metabolites will be demonstrated on straight-phase systems.

References

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