sonnas, 1968). As *in vitro* methods with higher sensitivity have also been described (for review, see Bisset, 1968) a series of such compounds was investigated to see if agreement was good or bad between *in vitro* and *in situ* results and whether the *in vitro* method has other advantages.

The method was essentially that of Méndez-Bauer, Cabot & Caldeyro-Barcia (1960). Mammary gland strips from rabbits fifth day post-partum were suspended in 10 ml. organ baths; their contractions were registered by Statham Gold Cell transducers and a Texas recorder. The resting tension was 500 mg. Standard oxytocin concentrations were 0·2 and 0·4 m-u./ml.; all doses were given at 10 min intervals and allowed to act for 2 min. The bath was washed out for 15 sec. A 4-point assay design (Schild, 1942) was used.

Results are given as i.u./μmole in Table 1 (column 3). *In situ* values are given in column 2 and ratios of oxytocic to pressor activity (isolated rat uterus and rat blood pressure) in column 5 (from Berde & Boissonnas, 1968). The *in vitro* values found are not far from but not identical with *in situ* results.

Substances with vasoconstrictor activity such as adrenaline and vasopressin are known to modify the *in vivo* responses of the mammary gland to oxytocin (for review see Bisset, 1968). The ratio in column 5 lists the substances to take account of the degree of their pressor activity. An inhibitory effect *in situ*, due to vasoconstriction, might cause the *in vitro* values for strongly pressor substances to be higher. Such a trend is recognizable but does not apply to all compounds. Vasoconstrictor activity may be one—though not the only—factor interfering in the *in situ* method.

Advantages of the *in vitro* method were (*a*) it appears to be free of possible influence of vasoconstrictor activity; (*b*) it allows definite values to be obtained where this is impossible *in situ*.

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Modification by phospholipids of responses of the guinea-pig isolated ileum to drugs and transmural stimulation

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Cell membrane phospholipids include cephalin (phosphatidylethanolamine and phosphatidyl-L-serine) and lecithin (phosphatidylcholine). Since these phospholipids appear to play an important part in the control of membrane permeability and ionic transport (Tobias, Agin & Pawlowski, 1962; Wolfe, 1964), it was considered of interest to study their effect on the longitudinal contractions of the guinea-pig isolated ileum preparation promoted either by agonistic drugs or by transmural stimulation.

Pieces of ileum from adult female guinea-pigs were suspended in Tyrode solution, at 30° C, gassed with air. Responses to acetylcholine approximately 50% of maximum were obtained; these were potentiated by addition of cephalin (10 μg–1 mg/ml.) to the bathing solution. The cephalin used in our experiments was a crude extract consisting of phosphatidylethanolamine and phosphatidyl-L-serine, and each of these phospholipids likewise potentiated the acetylcholine response. Phosphatidylethanolamine was approximately as effective as cephalin in this respect, but phosphatidyl-L-serine had much less activity. With each of these phospholipids a slight inhibition usually preceded the potentiation of the acetylcholine response. When larger concentrations (>250 μg/ml.) of the phospholipids were used the potentiation was often accompanied by a direct contractile effect.

A reverse sequence to the above events was observed with phosphatidylcholine (lecithin). In contrast to cephalin and its constituents the predominant effect of this phospholipid was inhibition of the acetylcholine response. A subsequent batch of lecithin (a crude extract from egg yolk) produced different results, but a sample of chromatographically pure synthetic dipalmitoyl phosphatidylcholine confirmed the original observations.

The effects of the phospholipids were not specific for acetylcholine, as cephalin, phosphatidylethanolamine and phosphatidyl-L-serine also potentiated the responses to histamine, 5-hydroxytryptamine, tetramethylammonium, potassium and barium ions, and to transmural stimulation. Lecithin inhibited these responses. High (up to 5 times normal) concentrations of Ca^{++} in the bathing solution prevented the potentiation by cephalin of responses to acetylcholine and transmural stimulation, whilst inhibition by lecithin was unaffected or increased. Conversely, low (1/3 to 1/10 of normal) Ca^{++} concentration increased the potentiation by cephalin but prevented the inhibition by lecithin.

Rojas & Tobias (1965) reported that at physiological pH, phosphatidylethanolamine binds Ca^{++} whilst phosphatidylcholine (lecithin) weakly repels Ca^{++}. Although the modes of action of cephalin and lecithin on the guinea-pig ileum are at present unclear, some pharmacological involvement is indicated between these compounds and calcium ions.

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A non-adrenergic component to the inhibitory innervation of the fundus of the rat stomach

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Inhibitory innervation which does not have the characteristics of adrenergic innervation has been described for the taenia of the guinea-pig caecum (Burnstock,