probable, therefore, that if milder fractionation procedures could be devised a lipovitellin containing much more total lipid and a greater proportion of neutral lipids might be obtained.

SUMMARY

1. The lipid of lipovitellin contains a much higher proportion of phospholipin than does total egg-yolk lipid, but their respective phospholipins have similar proportions of phosphatidylcholine, phosphatidylethanolamine and unsaturated fatty acids.

2. The fatty acids of the phospholipins of total yolk lipid and of lipovitellin are considerably more unsaturated than are those of the corresponding glycerides.

3. Lipovitellin contains much less cholesterol than the lipoproteins of human serum and appears to be considerably more stable.

4. Analysis of fractions of the lipid which became extractable by solvents after various treatments involving freezing or drying showed that non-phospholipin was removed most readily, followed by phosphatidylethanolamine, but there was no clear-cut separation of the constituents.

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Etherification of Noradrenaline in Acidified 95 % Ethanol. (±)-2-Ethoxy-2-(3':4'-dihydroxyphenyl) ethylamine hydrochloride

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In the course of pharmacological and chemical studies on noradrenaline in these laboratories, it was observed that (–)-noradrenaline hydrogen tartrate on standing in 95 % ethanolic hydrochloric acid (1 ml. of concentrated hydrochloric acid plus 99 ml. of 95 % ethanol, hereinafter referred to as 'acid alcohol') showed evidence of forming a new compound. This evidence consisted of appearance of a second, faster-travelling spot in an ascending paper chromatogram using *n*-butanol saturated with 0.5N-hydrochloric acid as solvent and ferricyanide (James, 1948) as indicator. Since the new derivative had been formed in an acid medium it was felt that

the compound arose by reaction of the side-chain hydroxyl group. This type of reactivity was demonstrated by Tullar (1948) who has found that (±)-noradrenaline is almost quantitatively converted to its methyl ether by evaporating *in vacuo* a solution of the hydrochloride in methanol. Accordingly, it seemed reasonable to expect some ether formation on merely allowing noradrenaline to stand in acidified 95 % ethanol as well as on concentrating such solutions. It therefore was desired to synthesize the indicated ethyl ether and to demonstrate its formation under the conditions given.

Table 1. Duplicate results of ascending paper chromatograms using *n*-butanol saturated with 0.5*N*-hydrochloric acid

(The colour of all spots was pink-lavender.)

	Lane 1 Residue of ethanolic-HCl soln. of noradren- aline hydrochloride in 0.01 <i>N</i> -HCl <i>R_F</i>	Lane 2 (±)-Noradrenaline ethyl ether hydrochloride in 0.01 <i>N</i> -HCl <i>R_F</i>	Lane 3 (±)-Noradrenaline hydrochloride in 0.01 <i>N</i> -HCl <i>R_F</i>	Lane 4 Acid-alcohol soln. (3½ months old) of (–)-noradrenaline hydrogen tartrate <i>R_F</i>
Spot I	0.063	—	0.067	0.071
Spot II	0.39	0.39	—	0.40

EXPERIMENTAL

(±)-Noradrenaline ethyl ether hydrochloride (2-ethoxy-2-(3':4'-dihydroxyphenyl) ethylamine hydrochloride). One-half gram of (±)-noradrenaline hydrochloride (Winthrop-Stearns, Inc.) decomposition point 138–139°, was dissolved in 50 ml. of absolute ethanol (dried over magnesium ethoxide) with slight shaking and warming. The solution was saturated with HCl gas with slight cooling; a few, small, needle-like crystals precipitated during this operation. The mixture was evaporated to dryness under reduced pressure in a current of N₂ at room temperature. The colourless, oily residue on standing in a desiccator turned yellow-orange. On scratching with a few drops of absolute ethanol and chilling in a dry-ice bath, crystallization occurred. Addition of ether with scratching yielded 0.39 g. of solid (69% yield); careful addition of ether to an ethanolic solution of the solid yielded rosettes of colourless needles. Repeated crystallization of the crude solid from ethanol-ether gave a solid melting with decomposition at 171–172° (corr.) to an orange-brown, frothy solid (capillary placed in bath at 165°). An aqueous solution of this compound gave a dark-green coloration with ferric chloride. [Found: C, 51.6; H, 7.0; N, 6.3. C₁₆H₁₉O₃N·HCl requires C, 51.4; H, 6.9; N, 6.0%. (Analyses by Elek Microanalytical Laboratory, Los Angeles, California.)]

Paper chromatography. Whatman no. 1 filter paper was used; sheets were placed in a glass jar, the bottom of the paper being placed in *n*-butanol saturated with 0.5*N*-HCl; a beaker of the same solvent was also placed in the jar. The papers, ruled in four lanes, were allowed to develop 22½ hr., then dried ½ hr. The dried papers were sprayed with 0.44% potassium ferricyanide in pH 7.8 phosphate buffer. In all lanes the total amounts of compound added were equivalent to 10 µg. of free base. In lane no. 1 was applied 0.01 ml. of a 0.01 *N*-HCl solution of the residue formed by evaporating *in vacuo* (±)-noradrenaline hydrochloride in ethanol to dryness at 60–65°. The ethanol had been distilled from NaOH and contained 0.05 ml. of conc. HCl per 100 ml. (Crawford, 1951). Lane no. 2 contained 10 µg. of (±)-noradrenaline ethyl ether and was applied in 0.01 ml. of 0.01 *N*-HCl. In lane no. 3 was placed 0.01 ml. of a freshly prepared solution of (±)-noradrenaline hydrochloride in 0.01 *N*-HCl. Lane no. 4 contained 0.01 ml. of a 3½-month-old acid-alcohol solution of (–)-noradrenaline hydrogen tartrate; the original

solution, refrigerated since its preparation, contained 10 µg. of free noradrenaline per 0.01 ml.

The results of duplicate chromatograms appear in Table 1.

DISCUSSION

The *R_F* value and the colour given by noradrenaline ethyl ether were found to be the same as those of the fast-travelling spots given by old or evaporated ethanolic acid solutions of noradrenaline (Table 1).

Crawford (1951), on the basis of paper chromatographic evidence, found that adrenaline and noradrenaline undergo partial alteration during the evaporation of extracts of an adrenal medullary tumour in ethanolic hydrochloric acid. He pointed out that the new compounds were artifacts and suggested that they were lactyl derivatives.

On the basis of the relative ease with which noradrenaline appears to undergo ether formation in 95% ethanolic acid solutions, the possibility of error in concentrating such solutions or allowing them to age prior to assay should be emphasized.

As a matter of routine interest the pressor activity of the noradrenaline ethyl ether hydrochloride on the cat's blood pressure was determined and it was shown to have an activity of 0.004 (noradrenaline = 1), hydroxytyramine (2-(3':4'-dihydroxyphenyl) ethylamine) having an activity of 0.01 on the same preparation.

SUMMARY

1. (±)-Noradrenaline ethyl ether hydrochloride was synthesized.

2. Results of paper chromatography indicate that concentration or ageing of 95% ethanolic acid solutions of noradrenaline lead to reaction of the side-chain hydroxyl group to give the ethyl ether.

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