site of this tissue factor have shown it to be present in brain, kidney, liver, lung and muscle; it is concentrated in the supernatant after differential centrifugation and is not released by 0·1 per cent (v/v) 'Triton *X*-100'. Using 2-fold dilutions we have shown that the ability of tissue extracts to form fibrin *i* exceeds by many times that of blood, so that our results are not due to contaminating blood fibrinase. Further experiments are in hand to determine the possible relationship between the anti-fibrinolytic and the fibrinase-like activities of tissue extracts.

At this stage, it can only be pointed out that the existence of a tissue fibrin-stabilizing factor must be recognized and possibly taken into account when interpreting results relating to anti-fibrinolytic activity in tissue extracts. Such activity is possibly not due to tissue anti-plasmin. The recognition of a tissue fibrin-stabilizing factor may assist in the investigation of pathological conditions where deposition and persistence of fibrin occur.

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Oxidation of Glutathione and Other Thiols by the Xanthine Oxidase and Hypoxanthine of Rat Liver Homogenates

Glutathione (GSH) is rapidly oxidized to GSSG when incubated in a rat liver homogenate. The reaction is enzymatic since it is largely prevented by previously heating the homogenate[1,2]. The following observations have now been made (Table 1).

(1) Oxidation of GSH is abolished by previous dialysis of the homogenate and restored 70–90 per cent by adding to the dialysed homogenate a neutralized protein-free supernatant (PFS) obtained by precipitating proteins (with metaphosphoric acid) from an undialysed homogenate.

Table 1. Effect of AHFP and Hypoxanthine on the Oxidation GSH at *p*H 7·4 and 37° in Media derived from a Rat Liver Homogenate

Medium	GSH loss (μmole/ml.)
Homogenate + buffer	0·87
Homogenate + AHFP	0·08
Protein-free filtrate (PFF)	0·08
Dialysed homogenate:	
+ Buffer	0·02
+ PFF	0·59
+ Hypoxanthine (0·17 μmole/ml.)	0·63
+ Hypoxanthine (0·5 μmole/ml.)	1·77
+ AHFP + hypoxanthine (0·17 μmole/ml.)	0·06

1 vol. of 20 per cent homogenate (prepared in phosphate–saline buffer) added to 1 vol. of the same buffer containing the other components. GSH concentration, 2 μmoles/ml.; loss estimated after 30 min with Ellman's reagent (ref. 2).

(2) Hypoxanthine substitutes for PFS. The rate of oxidation of GSH increases with increasing hypoxanthine concentration.

(3) The specific xanthine oxidase inhibitor, 2-amino-4-hydroxy-6-formylpteridine[3] (AHFP), inhibits 90–95 per cent the oxidation of GSH by the undialysed homogenate or by the dialysed homogenate plus hypoxanthine.

In accordance with the known properties of xanthine oxidase[4], cyanide (10^{-3} M) inhibits the oxidation by 60 per cent and arsenate (10^{-2} M) by 20 per cent while azide (10^{-2} M), fluoride (2×10^{-2} M) and carbon monoxide have no inhibitory effect.

Fridovitch and Handler[5] have previously shown that sulphite and cysteine are oxidized by free radicals produced during the oxidation of hypoxanthine by xanthine oxidase in dog liver homogenate. The present results show that almost all the oxidation of GSH which occurs in rat liver homogenates is coupled to this system.

The oxidation of some other thiols in the homogenate and the effect of AHFP on the rate has been investigated (Table 2).

Table 2. Inhibitory Effect of AHFP on the Oxidation of Various Thiols in a Rat Liver Homogenate

Thiol added	Loss of thiol (μmole/ml.) Homogenate + buffer	Homogenate + AHFP	Percentage inhibition of oxidation
GSH	0·69	0·05	93
Cysteine	0·52	0·23	55
Homocysteine	0·79	0·26	67
Cysteamine	0·72	0·29	60
Thioethanol	0·65	0·12	81
Thioglycollate	0·69	nil	100

After adding 1 μmole/ml. of the thiol and EDTA (10^{-4} M) the thiol content was estimated immediately and after 30 min/37°. The corresponding endogenous GSH content of the homogenate (determined separately) was subtracted. Other conditions as in Table 1.

The xanthine oxidase system contributes substantially to the oxidations, its effect being greatest with GSH and thioglycollate and least with cysteine. Ascorbic acid is not significantly oxidized by rat liver homogenate.

Table 3. Protein-SH Group Content of a Rat Liver Homogenate after Incubation with or without AHFP

Incubation period 37°	Protein SH groups (μmole/ml.) Homogenate + buffer	Homogenate + AHFP
Nil	1·12	1·06
24 min	0·68	1·13
48 min	0·71	1·16

Protein-SH groups estimated as described in ref. 2.

AHFP also prevents the loss of the oxidizable part[2] of the homogenate protein SH groups (Table 3). This effect could be direct or a result of inhibiting the oxidation of endogenous GSH since the latter is known to protect protein-SH groups from oxidation[2]. In either case, the results suggest that addition of AHFP to homogenates might reduce losses in the activity of SH enzymes during their isolation.

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PHYSIOLOGY

Entry of a Dye into the Sarcotubular System of Muscle

It has been suggested on several grounds[1–5] that, in the striated muscle fibres of frogs, some part of the 'triads'[6] of the sarcoplasmic reticulum (presumably the middle element) is in some degree continuous with the external fluid as regards conduction of electricity and diffusion of