cortex[7] but the reticular activating system (RAS) must intervene greatly because higher levels of attention are associated with large-amplitude SCRs[6] and also because SCR itself is obtained by stimulation of RAS[8]. IPSH could therefore be considered as an index of the level of behaviour arousal during monotonous sollicitation.

In the present method, amphetamine sulf. (i.p.) is significantly active even at such a low dose as 0.06 mg/kg, while 5 mg/kg are necessary to increase locomotor activity (LA). Similarly pyrisuccideanol dimal. delays habituation at doses between 0.250 and 1 g/kg – a range where no LA increase is to be seen.

The IPSH-method is therefore more sensitive than LA-tests as far as the drugs used are concerned. In addition, it must be pointed out that the sought-after medical effect of psychoanaleptics is the maintenance of high arousal and attention capacity rather than muscular hyperactivity. Thus, even though species differ in response, the IPSH-test probably has a more predictable value than LA-tests in the search for psychoanaleptics. Moreover, contrary to EEG-tests, IPSH-test needs no special preparation and allows systematic studies on numerous batches of animals. Finally, habituation is, with sensitization, one of the most elementary forms of behavioral plasticity[9] and may also be considered as a special kind of conditioning[10]. The IPSH-test has thus proved itself a useful tool in psychopharmacological research.

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Antifibrinolytic Properties of Oxyphenbutazone in vitro

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Summary. The authors found that oxyphenbutazone (Tanderil®) added to culture medium, in amounts giving a final concentration of 10–100 μg/ml, causes a decrease in the liberation of fibrinolytic agents from explants of various tissues cultured in vitro.

The demonstration of fibrinolytic activity in tissue cultures in the early thirties prompted the first studies on tissue fibrinolysis (Fischer[1]; Santesson[2]). In recent years attention has again been focused on the fibrinolytic properties of tissue cultures (Bernik and Kwaan[3]; Åstedt and Pandolfi[4]; Åstedt et al.[5]) in an endeavour to find a model for studying the synthesis of fibrinolytic enzymes in the tissues and the mechanism of liberation of these agents from the cells. A method has recently been devised in which organ explants are cultured in the presence of standardized clots (Åstedt et al.[6] 1971). The advantage of this method is that fibrinolytic activators can exert their effect as soon as they are released into the medium, i.e. before they are inactivated (Åstedt and Pandolfi[4]). The amount of fibrinolytic agents released is indirectly assessed by immunochemically assaying the fibrin degradation products (FDP) accumulated in the culture medium. This method is a good experimental model for studying the mechanism of release of fibrinolytic activators from cells. Information on this phenomenon is valuable since cumulative evidence indicates that liberation of fibrinolytic agents from the active structures of tissues plays a role in the pathogenesis of thrombosis (Nilson and Isacson[7]), in inflammation (Donaldson[8] 1970) and in tissue repair processes (Astrup[9]).

This paper is a preliminary report on the depressive effect of an anti-inflammatory substance, oxyphenbutazone (Tanderil®) on the fibrinolytic activity of tissue cultures.

Material and method. Kidneys were obtained from newborn albino rats. In one case an extirpated cancer of the ovary served as donor material. The tissue fragments were washed in Parker 199 culture medium (SBL, Stockholm, Sweden) and divided into pieces about 1 mm across. These explants were then placed on slices of gel foam (Spongostan, Ferrosan, Malmö, Sweden), as a rule 3 explants per slice. The slices of gel foam with the explants were transferred to Leighton tubes (2 slices in each tube) containing Parker 199 (1.5 ml as a rule) culture medium. A 4 cm long glass tube (outer diam. 3 mm, inner 1.5 mm) open at one end was then inserted into the Leighton tube. This tube was filled with a mixture of 1 ml human plasminogen-rich fibrinogen (Kabi, dissolved in distilled water) and a minimal amount of bovine thrombin (Topostasin Roche, 7.5 NIH U/ml 0.15 *M* NaCl) resulting in a cylinder of fibrin occupying the cavity of the tube. In one experiment a 1 ml standard human fibrin clot at the end of the Leighton tube was used as substrate (Åstedt et al.[6]).

During culture of active tissues, the fibrin cylinder dissolved progressively from the open end of the glass tube. At certain intervals (12 or 24 h) 0.06 ml of the culture medium was collected and examined immunochemically for FDP (Niléhn[10]). Oxyphenbutazone was added to the

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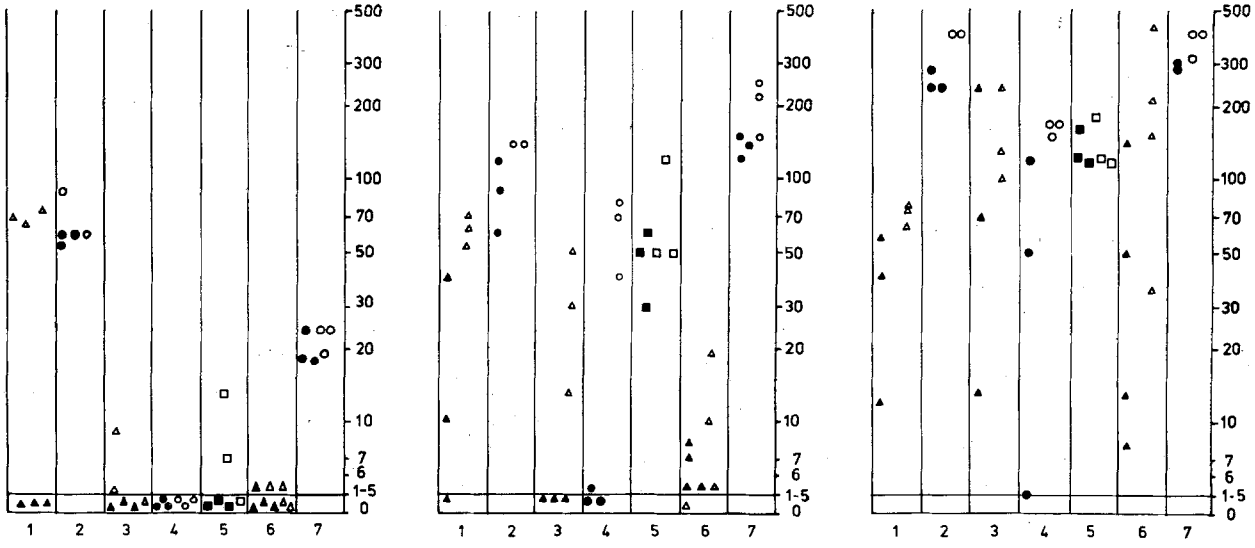

Fig. 1, 2 and 3. FDP in the medium of organ cultures treated and not treated with oxyphenbutazone in various concentrations 24, 48, 72 h respectively after the beginning of the culture. Ordinate (logarithmic): FDP in μg/ml. Abscissa: Number of the culture. Cultures 1, 2, 3, 4, 5 were made of newborn rat kidney; 6 of ovarian cancer. In culture 7 the substrate was a standard fibrin clot of 1 ml. ▲, ●, ■, denote cultures containing oxyphenbutazone in the medium in concentrations of 100, 50, 10 μg/ml, respectively. △, ○, □, denote corresponding controls. The cultures treated with oxyphenbutazone showed a fibrinolytic activity lower than that of the untreated cultures.

culture medium to reach a final concentration ranging from 10 to 100 μg/ml medium. Controls without oxyphenbutazone were run at the same time.

Results and comment. Besides a few pilot studies, 7 culture experiments were run based on a altogether 43 separate cultures. The lysis produced by the explants 24, 48, and 78 h after the beginning of the culture expressed in μg of FDP/ml medium is shown in Figures 1, 2 and 3. There is a progressive increase of FDP in the culture medium due to the continuous fibrinolysis.

The fibrinolytic activity of the cultures containing oxyphenbutazone in the medium was generally lower than that of the control cultures. Statistical analysis (Student's *t*-test) of the cultures with 100 μg oxyphenbutazone/ml (Nos. 1 and 3) and with 50 μg/ml (Nos. 2 and 4) showed a significant ($p < 0.02$) difference for the 100 μg/ml cultures after 24 h and 48 h. A lower fibrinolytic activity was also shown by the cultures of ovary cancer (No. 6) and in one where a preformed 1 ml fibrin clot was used (No. 7).

The results showed that oxyphenbutazone in a concentration of 10 μg–100 μg decreases the release of fibrinolytic agents from the cultures of embryonic and tumoral tissues resulting in a delay in the appearance of the dissolution of fibrin[11].

Hypothetically, the effect of oxyphenbutazone on the fibrinolytic activity of the cultures can be attributed to a stabilizing action of the drug on intracellular membranes, which would be followed by a decreased diffusion of fibrinolytic agents from the cells into the culture medium. This means that in this respect the action of oxyphenbutazone would resemble that found by HENRICSON[12] for cortisone.

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Studies on the Role of Phenethylamine in Methylamphetamine Action Mechanisms

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Summary. According to our results, we think that the tolerance developed to central effects of N-methylamphetamine are caused by the liberation and posterior depletion of phenethylamine from its storage places, which is in agreement with our hypothesis about the action mechanisms of amphetamines in the central nervous system.

Phenethylamine has been found in different animal organisms including man[1–4]. It is a homologue of amphetamine and produces similar pharmacological effects[1,5,6]. In contrast to amphetamine, phenethylamine is a substrate of monoaminooxidase[7]; for this reason it is often necessary to administer it together with a monoaminooxidase inhibitor in order to obtain satisfactory results. Phenethylamine has been postulated as a brain neurohumoral agent[6,8,9]. It can be produced by decarboxilation of its aminoacidic precursor phenylalanine and it is decomposed mainly by aminooxidation. Diminished urinary elimination of phenethylamine was found in certain forms of depressive disease, probably of endogenous origin[3,4]. Treatment of such patients with