Nevertheless, both, the leucotactic and the anaphylatoxin activity, are influenced in a different manner by the concentrations of the 2 peptides[21,22]. Therefore, leucotactic and anaphylatoxin effects represent different activity phases with only a partial overlap in certain concentration areas of the binary peptide system [21,22]. Thus, the homologous anaphylatoxin can act biologically (in terms of chemotaxis) as a component of the peptide system without displaying toxic effects itself (in terms of induction of lethal shock in vivo, and of guinea-pig ileum contraction in vitro). The evaluation of the existence of such partially overlapping activity phases of anaphylatoxin effects may explain physiological (e.g. mobilization of cellular defense mechanisms) and pathological reactions (e.g. some types of anaphylactic reactions) in which participation of anaphylatoxin in vivo is discussed (for review see[3,28]).

The anaphylatoxin (I) and the cocytotaxin (II) levels can be regulated by the activity of a leucotactic peptide system regulator enzyme (LSRE)[17]. This hitherto unknown enzyme, which has been highly purified[29], is most likely a peptidyl transferase or a ligase. The mechanism of action of this enzyme is under study, but it is conceivable that it catalyses a normal transpeptidation reaction as known from model studies[30,31]. In serum (hog, rat and guinea-pig), this enzyme is normally inactive, but it is activated by various particles with high surface activity[17] at neutral pH (e.g. certain lots of Sephadex G 25, certain types of chorcoal[29]). Active LSRE links the 2 peptides of the leucotactic peptide system, thus forming multiple proteins (refered as protein A, B, and C) with a molecular weight of 28,000, 56,000, and 112,000, respectively, as determined by gel chromatography[29]. The first hitherto identifiable product of enzymatic catalysis is protein A.

The isolated 3 proteins as metabolic products of anaphylatoxin and cocytotaxin show no chemotactic activity for neutrophils, neither alone nor in combination with anaphylatoxin or cocytotaxin[32]. In view of the fact that these proteins also contain the anaphylatoxin moiety, they were assayed for anaphylatoxin-like activities[32]: Protein A (mol. wt. 28,000) has similar activities to anaphylatoxin peptide (I). Shock induced by anaphylatoxin on guinea-pigs results in death after 4–5 min with histamine liberation and lung emphysema (preventable by antihistamines), whereas protein A causes a fatal shock with death after 5–8 min without formation of lung emphysema. Nevertheless, the behaviour of the animal resembles the behaviour during anaphylatoxin shock. Typical symptoms are dyspnoea and spasms. Protein B and C cause protracted lethal shock with death after 40–60 min or 2–12 h, respectively. Typical symptoms of this protracted shock are successive and alternating appearance of dyspnoea, excitation, sleep and drowsiness and, depending on the applied concentration of proteins, screaming spasms. Death is caused by circulatory insufficiency with symptoms of right ventricle dilatation and edema (especially after application of protein B, mol. wt. 56,000). Shocks induced by protein A, B or C cannot be prevented by antihistamine or protease inhibitors. The physiological function of these proteins is at present unclear, but obviously, they produce shocks which are similar to those protracted shocks observed in experimental anaphylaxis[3,33,34].

With the isolation of different mediators of shock on guinea-pig, many reported contradictory results on the biological action of anaphylatoxin preparations which have been produced by different contact substances (for review see[2,3]), might be explained by the interplay of different mediators, formed as a consequense of enzymatic reaction with anaphylatoxin as one of the substrates. Evidence remains to be established as to how far the isolated components of this system are activity principles in similar phenomena in vivo, such as the Arthus reaction for which the participation of anaphylatoxin is discussed[3,28], and the Shwartzman phenomenon[35]. Otherwise, on the basis of the biological activities of the reported components of the leucotactic peptide system, a hitherto unrecognized mediatory relationship is suggested between chronic inflammation, anaphylatoxic and other pathological reactions with symptoms of circulatory insufficiency and cardiac disease[36,37].

Zusammenfassung. Produkte einer enzymatischen Reaktion mit klassischem Anaphylatoxin als Substrat, das als Peptidkomponente des leukotaktischen Systems identifiziert und kristallisiert wurde, können als Mediatoren verschiedene Typen des protrahierten Schocks verursachen.

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Radioprotective Effectiveness of Some Serotonin-Like Compounds

Recently it was shown[1] that some sulphur analogues of 5-hydroxytryptamine (serotonin) gave good protection in supralethally irradiated mice. The radioprotective effectiveness of 5-mercaptotryptamine, as well as of so-called 'sulphur analogue of serotonin' [SAS, i.e. 3-(β-aminoethyl)-5-hydroxy-benzo(b)thiophene][2], was close to that of serotonin. Furthermore, 5-methoxytryptamine was found to be also a potent radioprotector in mice[3,4], rats[5] and, to a certain degree, in Rhesus monkies[6]. Therefore it seemed worthwhile to examine 2 other

serotonin-like compounds: 5-ethoxytryptamine[7] and 5-methoxy-SAS[8] (5-methoxytryptamine molecule in which the nitrogen atom in the ring is substituted by sulphur). In the available literature there are 2 short reports on the first substance indicating its high toxicity[4] and modest radioprotectiveness[6], while there are no data on 5-methoxy-SAS.

In the present experiment, due to the restricted amounts of both substances, only one dose of irradiation was applied. Therefore mice (F_1 hybrids of CBA ♂ and C 57 Black ♀) were irradiated with a distinctly supralethal dose of X-rays, i.e. 1400 R ($LD_{100/30}$ = 950 R). For the same reason, it was impossible to test previously the toxycity of these compounds. The substances in question were administered i.p. 5–10 min before irradiation in doses equimolar to the optimal dose of 5-hydroxytryptamine (50 mg/kg body wt.)[10]. Every experimental group numbered 20 mice. The survival of irradiated animals was followed for 30 days.

The results indicate (Table) that 5-ethoxytryptamine and SAS are protective to the same level. This radioprotective effectiveness apears to be insignificantly lower than that of 5-methoxytryptamine. The χ^2-test for 5-ethoxytryptamine, as compared to serotonin, was not significant. The difference in effectiveness between 5-methoxytryptamine and serotonin is negligible. As for 5-methoxy-SAS, it does not exhibit any radioprotective effect in supralethally irradiated mice.

In spite of the preliminary character of these findings, due to the small number of animals in each experimental group, it could be concluded that the substitution of the hydroxy group in position 5 of the indole ring by a methoxy, ethoxy or mercapto group is without any essential influence on the radioprotective effectiveness. Similarly, in the case of SAS, which has instead of the indole ring a benzothiophen nucleus, protection comparable to that of serotonin was observed. However, if in the molecule of SAS at position 5 the hydroxy-group is substituted by a methoxy group, its radioprotective property, under conditions of supralethally irradiation, completely disappears.

Whole-body irradiation of mice with 1400 R of X-rays ($LD_{100/30}$ = 950 R)

0.28 mM/kg body wt. (i.p.5–10 min before irrad.)	No. of animals	No. of survivors after 30 days	Mean survival time (± S.E.M.) in days
1) 5-Ethoxytryptamine	20	11 (55%)	20.3 ± 2.8
2) 5-Methoxytryptamine	20	15 (75%)	23.9 ± 2.0
3) 5-Hydroxytryptamine	20	17 (85%)	26.6 ± 1.9
4) 5-Methoxy-SAS	20	—	5.3 ± 0.6
5) SAS[a]	20	11 (55%)	20.8 ± 2.2

1):3) - χ^2 = 2.976, n.s. [a] 3-(β-aminoethyl)-5-hydroxy-benzo(b)thiophen (CAMPAIGNE et al.[2]).

To comment these finding it could be stated that all these substances elicit a radioprotective effect mainly through their specific pharmacological activity. Namely, 5-methoxytryptamine[11–13], as well as SAS[14,15], are pharmacologically very active compounds. The above-mentioned toxicity of 5-ethoxytryptamine[4] in the present experiment was not expressed. Some preliminary tests performed with 5-ethoxytryptamine and 5-methoxy-SAS indicate a rather weak pharmacological activity of these two compounds[16].

Future studies concerning the relationship between chemical structure, radioprotective effectiveness, pharmacological and toxicological activity might lead to a better understanding of the radioprotective mechanism of these substances.

Zusammenfassung. Bei Mäusen wurde die Strahlenschutzwirksamkeit des 5-Ethoxytryptamins und 5-Methoxytryptamins mit derjenigen von 5-Hydroxytriptamin, SAS (Benzothiophenverbindung) und 5-Methoxy-SAS verglichen. Die Ergebnisse zeigen, dass die Schutzwirksamkeit des 5-Ethoxytryptamins der des SAS sehr ähnlich ist.

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Apurinic Acid, a Modified DNA with Anticancer Activity

In 1952, TAMM, HODES and CHARGAFF reported the production of a purine-free DNA, termed apurinic acid (APA), after subjecting DNA to mild acid hydrolysis[1]. In place of the detached purine bases, APA has an equivalent number of free aldehydo groups[2]. In view of the finding that exogenous, macromolecular DNA can be incorporated into mammalian cells[3–5], we were prompted to consider whether APA possesses any biological activity. In particular, could APA disturb cell proliferation in vivo?

APA was prepared from herring sperm DNA by a method described in detail elsewhere[6]. Briefly, DNA was acidified to a pH of 2.5, quickly brought to boil, and then