saline, and collected by centrifugation. The total amount of protein precipitated was estimated by the Kjeldahl method. Similarly, the crossreaction between poly-(tyr.-glu.ala.gly)gly-1-C^{14} ethyl ester and the antisera to poly-(tyr.glu.val.gly)gly-1-C^{14} ethyl ester was performed, and similar series of precipitin reactions were observed (Fig. 1).

Since both of these antigenic polypeptides give similar precipitin reactions with the antisera to poly-(tyr.-glu.ala.gly)gly-1-C^{14} ethyl ester, it has been concluded that these atibodies are unable to differentiate between the alanyl and valyl residues. It has, therefore, been concluded that the alanyl residue is not part of the active site of its respective antigen. However, antisera to poly-(tyr.glu.val.gly)gly-1-C^{14} ethyl ester does seem to show more specificity for the sterically larger valyl residue than for the alanyl moiety.

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Antitumor Activity of An Acronycine–Polyvinylpyrrolidone Coprecipitate

Keyphrases ☐ Acronycine–polyvinylpyrrolidone coprecipitate—antitumor activity ☐ Antitumor activity—acronycine–polyvinylpyrrolidone coprecipitate

Sir:

Polyvinylpyrrolidone (PVP) is known to increase the solubility of aromatic compounds (1–3). This has been explained (1) as a result of hydrophobic bonding and an exothermic interaction between the solubilized compound and PVP. Application of this phenomenon to pharmaceuticals has been demonstrated (2, 3), and the advantages of PVP–drug coprecipitates as superior systems for pharmaceutical applications are known (4, 5).

In our work, pharmaceutical grade, 40,000 molecular weight, PVP was coprecipitated with acronycine from ethanol. The ratio of acronycine to PVP was 1:5 (w/w). Solubility of acronycine as the coprecipitate (75 mcg./ml., distilled water) was approximately 15 times that of noncoprecipitated acronycine (5 mcg./ml.). Acronycine,[1] a compound of known experimental antitumor activity (6), was compared with the acronycine–polyvinylpyrrolidone (Ac–PVP) coprecipitate against two of the most sensitive tumors to acronycine, X5563 plasma cell myeloma and C1498 myelogenous leukemia (Table I). These data indicate that PVP coprecipitated acronycine is more active than acronycine itself. Efforts are continuing in this area to optimize acronycine activity by adjusting the acronycine to PVP ratio and by employing other molecular weight grades of PVP.

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[1] The United States Adopted Names Committee (USAN) has approved acronine as the generic name for acronycine.

Table I—Antitumor Activity of Acronycine and an Acronycine–PVP Coprecipitate

Sample	Tumor[a]	mg./kg. × Days Dosed[b]	Route	ATD, mm.[c]	ALS, Days[d]	I, %[e]	PL, %[f]
Acronycine	X5563	30 × 9	i.p.	8.3	—	52	—
Ac–PVP	X5563	180 × 9	i.p.	0.9	—	95	—
Control	X5563	Emulphor × 9	i.p.	17.2	—	0	—
Acronycine	X5563	45 × 9	Oral	6.8	—	46	—
Ac–PVP	X5563	270 × 9	Oral	0.0	—	100	—
Control	X5563	Emulphor + 9	Oral	12.5	—	0	—
Acronycine	C1498	30 × 10	i.p.	—	20.4	—	40
Ac–PVP	C1498	180 × 10	i.p.	—	23.6	—	62
Control	C1498	Emulphor × 10	i.p.	—	14.6	—	0
Acronycine	C1498	45 × 10	Oral	—	19.4	—	24
Ac–PVP	C1498	270 × 10	Oral	—	24.2	—	55
Control	C1498	Emulphor × 10	Oral	—	15.6	—	0

[a] X5563 was implanted by trocar, subcutaneously, in C_3H mice, and therapy was begun 72 hr. later. C1498 was transferred by an intraperitoneal injection of tumor homogenate, and therapy was begun 24 hr. later. [b] Ac–PVP was coprecipitated in a 1:5 w/w basis. Emulphor (General Aniline and Film, New York, N. Y.) was the suspension vehicle for both acronycine and Ac–PVP. [c] ATD = average tumor diameter of 10 animals expressed in millimeters. [d] ALS = average life span of 10 animals expressed in days. [e] % I = ATD of the treated/control expressed as a percent inhibition. [f] % PL = ALS of the treated/control expressed as a percent prolongation of life.