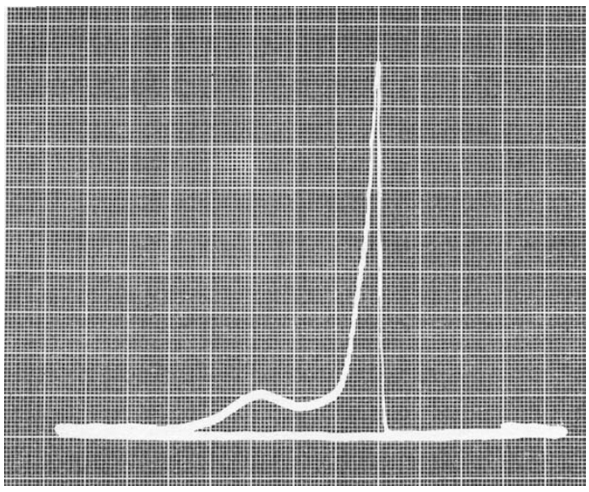


Fig. 2. Oscilloscope pattern of aquoluminescence from γ-irradiated NaCl.

cible by gamma irradiation (2×10^{19}/mole in NaCl). These results agree with values reported earlier[1-3]. The phenomenon thus seems to provide a relatively simple method for studying irradiation effects in crystals.

H. J. Arnikar
P. S. Damle
B. D. Chaure
B. S. Madhav Rao

Department of Chemistry,
University of Poona,
Poona-7, India.

Received April 22; revised July 20, 1970.

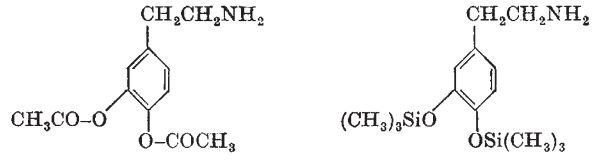
[1] Markham, J. J., Platt, jun., R. T., and Mador, I. L., *Phys. Rev.*, **92**, 597 (1953).
[2] Seitz, F., *Rev. Mod. Phys.*, **26**, 7 (1954).
[3] Alger, R. S., *J. Appl. Phys.*, **21**, 30 (1950).

BIOLOGICAL SCIENCES

Possible Dopamine Derivatives capable of Crossing the Blood–Brain Barrier in relation to Parkinsonism

The exact neurophysiological role of dopamine is still unclear, but it has been implicated in the functioning of the extrapyramidal motor system (EPS)[1,2]. Experiments on animals and humans, however, indicate that the smooth functioning of the EPS depends on a fine balance between several biogenic amines[3-5]. Nevertheless, deficiencies of brain dopamine resulting from degeneration of the substantia nigra seem to be associated with the extrapyramidal symptoms of Parkinson's disease[1-6]. In accordance with these observations, attempts have been made to raise brain dopamine levels in patients suffering from Parkinsonism. Dopamine itself cannot be used, for it is incapable of crossing the blood–brain barrier, and therefore dopamine precursors, in particular L-3,4-dihydroxyphenylalanine (L-dopa), have been used[7-10]. Although such treatment apparently relieves the symptoms of hypokinesia, rigidity and posture, tremor is little affected and the necessity for large daily dosage and the side-effects of nausea and hypotension remain as serious drawbacks to the therapeutic use of L-dopa. Stock[11] has recently suggested that 2-amino-4-hydroxy-6,7-dimethyltetrahydropteridine may be a potential anti-parkinsonism agent since this tyrosine hydroxylase co-factor may be deficient in patients suffering from Parkinsonism[12].

Implicit both in Stock's suggestion and in the use of L-dopa is the assumption that dopamine precursors capable of crossing the blood–brain barrier will be enzymatically transformed *in vivo* into dopamine, thereby increasing brain dopamine levels. I propose that such levels could more easily be increased by administration of labile, lipophilic derivatives of dopamine. The modification of pharmacological activity by the synthesis of labile derivatives which undergo either enzymatic or non-enzymatic hydrolysis *in vivo* to regenerate the parent drug is well known, and the principle has been successfully applied to noradrenaline[13]. The 3,4,β-triacetate and 3,4,β-*tris*-(trimethylsilyl) derivatives of noradrenaline cause the sustained release of the parent catecholamine in mouse brains[14]. It therefore seems likely that similar derivatives of dopamine, for example I[15] and II[16], may penetrate into



I II

the central nervous system and be converted to dopamine in the vicinity of the basal ganglia, for both *in vitro* and *in vivo* experiments[1,2] indicate that dopamine is preferentially taken up by these parts of the brain.

R. M. Pinder

Chemical Defence Establishment,
Porton Down,
Salisbury, Wiltshire.

Received March 25, 1970.

[1] Hornykiewicz, O., *Pharmacol. Rev.*, **18**, 925 (1966).
[2] Hornykiewicz, O., *Pharmako-psychiat. Neuro-psychopharmakol.*, **1**, 6 (1968).
[3] Friedman, A. H., and Everett, G. M., *Adv. Pharmacol.*, **3**, 83 (1964).
[4] Curzon, G., *Intern. Rev. Neurobiol.*, **10**, 323 (1968).
[5] Ernst, A. M., *Acta Physiol. Pharmacol. Neerl.*, **15**, 141 (1969).
[6] Barbeau, A., *Rev. Canad. Biol.*, **26**, 55 (1967).
[7] Calne, D. B., Stern, G. M., Laurence, D. R., Sharkey, J., and Armitage, P. *Lancet*, **i**, 744 (1969).
[8] Calne, D. B., Stern, G. M., Spiers, A. S. D., Laurence, D. R., and Armitage. P., *Lancet*, **ii**, 973 (1969).
[9] Cotzias, G. C., Papavasiliou, P. S., and Gellene, R., *New Engl. J. Med.*, **280**, 337 (1969).
[10] Godwin-Austen, R. B., Tomlinson, E. B., Frears, C. C., and Kok, H. W. L. *Lancet*, **ii**, 976 (1969).
[11] Stock, R., *J. Amer. Med. Assoc.*, **210**, 1594 (1969).
[12] Kuehl, F. A., Vandenheuvel, W. J. A., and Ormond, R. E., *Nature*, **217**, 136 (1968).
[13] Daly, J. W., Creveling, C. R., and Witkop, B., *J. Med. Chem.*, **9**, 273 (1966).
[14] Creveling, C. R., Daly, J. W., Tokuyama, T., and Witkop, B., *Experientia*, **25**, 26 (1969).
[15] Brooks, C. J. W., and Horning, E. C., *Anal. Chem.*, **36**, 1540 (1960).
[16] Horning, M. G., Moss, A. M., and Horning, E. C., *Biochim. Biophys. Acta*, **148**, 597 (1967).

Sunlight-induced Pyrimidine Dimers in Human Cells *in Vitro*

Pyrimidine dimers have been implicated in much ultraviolet light induced damage in bacteria[1], and it has been shown that they can be induced in mammalian cells with short wavelength ultraviolet light[2-7]. In placental mammals, pyrimidine dimers are not repaired by direct monomerization by photoreactivating light[2,8,9], although a dark repair mechanism, somewhat similar to that found in bacterial cells, has been demonstrated[10].