the bare zone of *S. leucophylla* contained only 5.26 g (dry weight) of plant material. Although this is an order of magnitude greater than the amount in either of the open-sided exclosures, this complete exclosure had less plant material than any of the other complete exclosures. This difference possibly results from this exclosure's being on a slope (whereas all the others were on level ground), the soil of which was undergoing sheet erosion. Consequently there would be fewer seeds under the exclosure for germination during the experiment.

Animal activity can possibly account for several characteristics of the bare zone. Outside the bare areas there is a region of partial inhibition of plant growth, which could be caused by volatile toxins (*8*). However, partial inhibition could also be caused by a decreasing gradient of grazing activity (Fig. 1). If an annual plant is repeatedly grazed, it may become stunted as the drought season progresses and water becomes limiting for growth. Also, although the annual may continue to produce a flowering stalk, it will lack some of the storage products that are available to an ungrazed plant.

Another characteristic of the bare zone is the prevalence of native perennial grasses (*9*). It has been suggested that adult plants are inhibited to a lesser extent than seedlings (*9*). Thus, if a perennial grass becomes established in the bare zone, it would not be as inhibited by volatile toxins as would annual grasses which must be reestablished every year. However, animal activity can also account for the maintenance of perennial grasses in the bare zone. These grasses need not reproduce by means of seeds every year, but can continue to produce tillers. Thus, seed foraging will not affect these grasses to the same extent as annual grasses. These perennial grasses are often cropped, probably by rabbits, but the grasses seem to be able to withstand this cropping. Another characteristic of the bare zone is the occurrence of seedlings of adjacent shrubs (*10*). These plants have secondary plant products, such as terpenes, phenols, and cyanide (*9*), which would decrease their palatability to herbivores. Therefore, they can become established in the bare zone while more edible plants cannot. Several authors have discussed the selective value of these secondary plant products as means of protection against herbivores (*11*).

Muller and co-workers have demonstrated that volatile toxins produced by some of the coastal sage and chaparral plants are toxic to germinating seedlings, and terpenes can be absorbed by lipids and adsorbed on soil particles (*8*). However, in these studies much higher concentrations have been used than are found under field conditions, and it has yet to be shown that volatile inhibitors of plant growth are present in sufficient concentrations to cause the bare zone under field conditions.

Neither *B. pilularis* (*12*) nor *A. fasciculatum* (*10, 13*) has been shown to contain volatile plant growth inhibitors, yet stands of both of these shrubs often have well-developed bare zones. *Adenostoma fasciculatum* contains water-soluble toxins, and it has been proposed that these chemicals cause the lack of annuals directly under shrubs of *A. fasciculatum* (*10, 13*).

The extent of the relative contribution of chemical and animal inhibition to the formation and maintenance of the bare zone needs further investigation. However, annuals will grow in the bare zone with either the presence or absence of volatile toxins if animal activity is excluded.

BRUCE BARTHOLOMEW
*Department of Biological Sciences,*
*Stanford University,*
*Stanford, California 94305*

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## Parkinson's Disease: Activity of L-Dopa Decarboxylase in Discrete Brain Regions

Abstract. *The activity of* L-*dopa decarboxylase was greatly reduced in the striatum, less so in the hypothalamus, and unchanged in the cortex of brains of patients with Parkinson's disease. However, it appears that even in the striatum enough activity remained to allow for the formation of dopamine from* L-*dopa in patients treated with large doses of* L-*dopa.*

Although the symptomatology of Parkinson's disease has been known for a long time, it was not until about 10 years ago that insight was obtained into the neurochemistry of this disease. Dopamine (3,4-dihydroxyphenylethylamine) has a characteristic distribution pattern within the mammalian brain; 80 percent of the total dopamine in the brain occurs in the subcortical extrapyramidal regions, notably the caudate nucleus, putamen, substantia nigra, and globus pallidus (*1*). In patients with Parkinson's disease the concentrations of dopamine (*2*) and its major metabolite homovanillic acid (*3*) in these regions of the brain are greatly decreased, most probably as a result of degeneration of the nigrostriatal dopaminergic neurons (*4*). The importance of the dopamine deficiency in the brains of patients with Parkinson's disease has resulted in the successful clinical application of L-3,4-dihydroxyphenylalanine (L-dopa), dopamine's immediate precursor, in the treatment of this disease (*5*).

The enzyme converting L-dopa to dopamine is L-dopa decarboxylase (E.C. 4.1.1.26) (*6*). We described a sensitive assay for the determination of L-dopa decarboxylase in autopsy

Table 1. Activity of L-dopa decarboxylase in regions of the brains of patients with and without Parkinson's disease. The controls are patients without any known neurological disease. Enzyme activity is expressed as the number of counts per minute (minus blanks) per milligram of protein. Blanks ranged from 15 to 30 count/min per milligram of protein. Results are the mean ± S.E.M. The numbers in parentheses are the number of patients analyzed.

| Brain area | L-Dopa decarboxylase activity | |
|---|---|---|
| | Control patients | Patients with Parkinson's disease |
| Putamen | 864 ± 271 (9) | 38 ± 10 (6) |
| Caudate nucleus | 641 ± 200 (10) | 55 ± 14 (6) |
| Hypothalamus | 238 ± 91 (4) | 72 ± 21 (3) |
| Temporal cortex | 39 ± 8 (9) | 20 ± 3 (5) |
| Cerebellar cortex | 33 ± 9 (7) | 38 ± 9 (6) |
| Subcortical white matter | | |
| Cerebral | 17 ± 4 (10) | < 5 (5) |
| Cerebellar | < 5 (5) | < 5 (5) |

material of the human brain (*7*). In brief, brain tissue was homogenized in ice-cold isotonic dextrose and then incubated for 20 minutes (37°C) in 0.1*M* phosphate buffer (*p*H 7.0) and 0.6 m*M* pyridoxal phosphate. Carboxyl-labeled D,L-dopa was then added (final concentration of $2.5 \times 10^{-3}M$), and after 2 hours the reaction was terminated by the addition of acid, causing the release of the evolved carbon dioxide. The latter was trapped in hyamine hydroxide and transferred to a scintillation vial for estimation of radioactivity. Blanks contained *p*-bromo-*m*-hydroxybenzyloxyamine (Brocresine), a potent inhibitor of L-dopa decarboxylase. In the present study we used this method to determine whether there are any abnormalities in L-dopa decarboxylase activity in the brains after death of patients who had suffered from Parkinson's disease (*8*).

The activity of L-dopa decarboxylase was greatly reduced in the caudate nucleus and putamen in the brains of patients with Parkinson's disease as compared with the values obtained from brains of patients not suffering from Parkinson's disease (Table 1). The decrease of the enzyme activity in the hypothalamus was less pronounced. No significant difference could be detected between the controls and patients with Parkinson's disease in respect to L-dopa decarboxylase in the cerebral and cerebellar cortex.

The decrease in L-dopa decarboxylase activity along with that of dopamine in the striatum from patients with parkinsonism suggests that a large proportion of this dopamine-forming enzyme is located in the nigro-striatal dopaminergic neurons that degenerate in parkinsonism. This conclusion is in agreement with the results obtained in animals with experimental brain lesions which interrupt the nigro-striatal dopaminergic neurons (*9*).

It is unknown whether the reduction in the striatal L-dopa decarboxylase activity in patients with parkinsonism occurs prior to, or as a consequence of, the degeneration of the substantia nigra and the nigro-striatal dopaminergic pathway. However, in relation to the beneficial action of L-dopa in Parkinson's disease, it should be noted that this enzyme is normally not rate limiting in the biosynthesis of dopamine (*10*). We found significant, although low, activity of L-dopa decarboxylase (5 to 10 percent normal) still present in the striatum from patients with Parkinson's disease. Therefore, sufficient amounts of dopamine may be formed from the administered L-dopa to functionally counteract the striatal dopamine deficiency and thus alleviate those symptoms of Parkinson's disease (akinesia, rigidity, and possibly tremor) which are assumed to be striatal in origin. This conclusion appears to be supported by our initial data (*11*) showing an elevation of homovanillic acid in the striatum of patients treated with L-dopa as compared with untreated patients. At present it is unknown whether the homovanillic acid was formed only in the surviving dopamine neurons or in other striatal structures—for example, the serotonin neurons; it should be noted, however, that the concentration of striatal serotonin was not significantly different between the two groups of patients (*12*). Since, however, the homovanillic acid concentration in the patients treated with L-dopa was also elevated in brain areas other than the striatum (*11*) (which is in agreement with the distribution pattern of the decarboxylase) the possibility exists that the striatum might not be the only site of the pharmacological effects or side effects, or both, of L-dopa.

K. Lloyd
O. Hornykiewicz
*Department of Pharmacology, University of Toronto,*
and *Clarke Institute of Psychiatry, Toronto, Ontario, Canada*

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## Antimalarials: Effects on in vivo and in vitro Protein Synthesis

Abstract. *The antimalarials quinine, chloroquine, primaquine, and quinacrine inhibited the uptake and incorporation of amino acids in vivo, but these drugs had considerably less effect on cell-free protein synthesis. The results indicate that the primary effect of the four drugs on protein synthesis is blocking of amino acid uptake by the cells.*

Inhibition of protein synthesis in vivo by antimalarial drugs has been observed in bacteria (*1*), in *Plasmodium knowlesi* (*2*), and in the ciliate protozoan *Tetrahymena pyriformis* (*3*). In these reports, however, it was proposed that this effect was the result of an indirect action of the drugs. Ciak and Hahn (*1*) and Polet and Barr (*2*) suggested that the inhibition of protein synthesis could be ex-