Leukocyte Histidine Decarboxylase: Properties and Activity in Myeloproliferative Disorders

By Stephen Krauss, Harriet S. Gilbert and Louis R. Wasserman

With the technical assistance of Gertrude Lurinsky

Earlier observations of elevated blood and urine histamine levels in myeloproliferative disorders have recently been confirmed and extended in this laboratory using a sensitive and specific spectrophotofluorometric assay. Whole blood and urine histamine content was demonstrated to be increased in uncontrolled polycythemia vera, “spent” polycythemia, and myelofibrosis with myeloid metaplasia. Leukocyte histamine content was also measured, since the histamine in whole blood in man is contained almost entirely within circulating leukocytes. Patients with active myeloproliferative states, including chronic myelocytic leukemia, who had elevated blood and urine histamine levels, had increased leukocyte histamine as well. When remission was induced by myelosuppressive therapy, elevated levels of whole blood, leukocyte and urine histamine fell, reaching normal in most cases. Increased leukocyte histamine content could result from increased formation of the amine, decreased release or intracellular catabolism, or some combination of the two processes. Since the only known pathway for histamine synthesis in mammals is by the intracellular decarboxylation of histidine, a study of the ability of normal leukocytes and those from patients with myeloproliferative disorders to decarboxylate histidine was undertaken to see if increased enzyme activity might account, at least in part, for the observed increases in leukocyte and urine histamine content in myeloproliferative states.

Materials and Methods

The patients studied consisted of ward, clinic and private patients with myeloproliferative disorders in varying states of disease activity and therapy currently being followed in the Department of Hematology of The Mount Sinai Hospital as part of a long-term study of...
these disorders. Control subjects included normal volunteers and patients with relative polycythemia. Criteria used for the diagnosis of polycythemia vera, “spent” polycythemia, myelofibrosis with myeloid metaplasia and relative polycythemia have been set forth previously. Patients with “spent” polycythemia included those with previously diagnosed polycythemia vera who showed a decrease of the red cell mass to normal levels or below in the absence of bleeding or myelo-suppressive therapy, and increasing extramedullary hematopoiesis as evidenced by an enlarging spleen and/or liver and a leukoerythroblastic blood picture. Chronic myelocytic leukemia was diagnosed according to standard hematologic criteria.

Whole blood histamine was determined spectrophotofluorometrically by the method of Shore et al., and urine histamine by the method of Oates et al. Leukocyte histamine was determined by the method of Shore et al., after preparation of a leukocyte-rich fraction as described previously. Using this method, results are expressed as μg. of histamine base per 10^9 myeloid cells, on evidence that the histamine content of lymphocytes and monocytes is negligible; the upper limit of leukocyte histamine content in normal subjects is 18 μg./10^9 myeloid cells. This value shows good agreement with the data of Lichtenstein et al., when the differences in methodology employed are taken into account. Direct basophil counts were performed on peripheral blood and leukocyte-rich fractions by the method of Moore and Watson.

**Leukocyte Enzyme Assay**

Histidine decarboxylase was assayed by a modification of the method of Levine and Watts which involves the trapping of C^14_02 formed during decarboxylation. A leukocyte fraction was obtained following dextran sedimentation of erythrocytes as in the preparation of leukocytes for histamine determination. Contaminating red cells were then removed by lysis in hypotonic saline. Leukocytes were subsequently suspended in acetate buffer, pH 5.4, disrupted by freezing and thawing six times, homogenized using a glass homogenizer with motor-driven teflon pestle, and then centrifuged at 30,000 g. for 20 min. at 4 C. In order to eliminate the effects of variation in substrate concentration on the enzyme determination, it was necessary to remove endogenous histidine. Thus, the supernatant obtained from centrifugation was placed on a Sephadex G25 column and eluted with distilled water. This protein-rich eluate constituted the enzyme preparation. Protein determinations on leukocyte supernatant were performed using the method of Lowry and ranged from 2-4 mg./ml.

The incubation mixture consisted of 1 ml. of enzyme preparation, pyridoxal 5'-phosphate (3.7 × 10^-5M), streptomycin sulfate (1.0 × 10^-4M) to suppress bacterial growth, sodium phosphate buffer (12.5 × 10^-2M, pH 6.0), L-histidine (2.5 × 10^-4M) and carboxyl-labeled C^14-DL-histidine* (0.5 μc. S.A. 10 mc./mM), with water added to a final volume of 2.0 ml. The blank consisted of the above mixture plus an excess (1 × 10^-4M) of a potent and specific histidine decarboxylase inhibitor, alpha-hydrazino-analog of histidine,† MK 785. In studies on L-aromatic amino acid decarboxylase inhibitor, alpha-hydrazino-analog of histidine,‡ MK 785, the incubation being continued for 30 minutes more after addition of acid.

A CO_2 trap consisting of a filter-paper wick soaked in Hydroxide of Hyamine (Packard Instruments) was suspended from the cap of the polyethylene incubation vial. Following completion of the incubation, the filter paper was placed in a glass vial with dioxane-based scintillation fluid and counted in a Packard Tri-Carb Liquid Scintillation Spectrometer.

*Carboxyl-labeled C^14-DL-histidine was purchased from Calbiochem, and carboxyl-labeled C^14-DL-dopa from New England Nuclear Corp.

†Alpha-hydrazino analog of histidine (MK 785) was donated by Dr. Clement A. Stone of the Merck Institute for Therapeutic Research, West Point, Pa.
Fig. 1.—Kinetic studies on leukocyte histidine decarboxylase. Note dependence of enzyme activity on enzyme concentration (A) (see text), substrate concentration (B), and pH (C). Graph D demonstrates that the reaction is linear for the first hour, thus justifying the selection of the one hour incubation time in the enzyme assay.

Enzyme activity was expressed as cpm./mg. of leukocyte protein after subtraction of blank.

To determine histidine decarboxylase activity of intact leukocytes, the cells were suspended in buffered Tyrode’s solution, pH 6.8, in a concentration of 30–50 x 10^6 leukocytes per incubation flask. In experiments on enzyme localization, fractionation of mixed leukocyte suspensions was performed by the method of Rabinowitz,16 as well as by a modification in which columns were packed with siliconized nylon wool in the same manner as the siliconized glass beads or glass wool as originally described.

RESULTS

Extracts from human leukocytes demonstrated the ability to decarboxylate histidine under the conditions of the assay. Activity ranged from 40–220 cpm./mg. protein. Using the rat stomach as a source of enzyme, 300–1500 cpm./mg. were obtained, values comparable to those of Levine and Watts with this tissue.

Kinetic studies on the leukocyte enzyme preparation are illustrated in Fig. 1. For a given leukocyte extract, the yield was dependent upon the protein concentration within the limits shown (Fig. 1 A). At concentrations below 1 mg. protein/ml., counts did not fall toward background levels, probably because the

*Fenwal “Leukopak.”
Table 1.—Histidine Decarboxylating Enzymes

<table>
<thead>
<tr>
<th>Location</th>
<th>Specific</th>
<th>Nonspecific</th>
<th>Leukocyte</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fetus</td>
<td>Rabbit stomach</td>
<td>Human Leukocytes</td>
</tr>
<tr>
<td>Rat Mast Cells</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone Marrow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guinea-pig</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Bone Marrow</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Bone Marrow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guinea Pig</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver, Kidney</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Substrate</td>
<td>Histidine</td>
<td>Histidine +</td>
<td>C(^{14})</td>
</tr>
<tr>
<td>Specificity</td>
<td>aromatic amino</td>
<td>aromatic amino</td>
<td>C(^{14})</td>
</tr>
<tr>
<td>acids (trypt, dopa)</td>
<td></td>
<td>acids (trypt,</td>
<td>Dopa</td>
</tr>
<tr>
<td>pH optimum</td>
<td>6</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Requirement for</td>
<td>++ + +</td>
<td>0</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Pyridoxal 5'-PO(_4)</td>
<td>++++</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Inhibitors</td>
<td>++ + +</td>
<td>+</td>
<td>++ + + +</td>
</tr>
<tr>
<td>MK 785</td>
<td>++ +</td>
<td>+</td>
<td>+ + + +</td>
</tr>
<tr>
<td>α-mel dopa</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

Additional properties exhibited by the leukocyte enzyme preparation are listed in Table 1, where they are compared with those of histidine decarboxylating enzymes studied in rodents. Leukocyte histidine decarboxylation was found to exhibit a pH optimum of 6.0, when a substrate concentration of 10\(^{-4}\)M histidine was employed. The reaction was dependent on the presence of pyridoxal phosphate as co-enzyme, being undetectable in its absence and reaching a maximum at a concentration of 3.7 \times 10^{-5}M. Since an enzyme which non-specifically decarboxylates several L-aromatic amino acids as well as histidine has been described,\(^{17-20}\) the specificity of leukocyte histidine decarboxylation was investigated. Using C\(^{14}\)-DL-dopa as substrate, decarboxylation was observed, maximal at pH 6.0, but not requiring pyridoxal phosphate for activity. In order to determine if more than one histidine decarboxylating enzyme was present, the effect of known inhibitors of the specific and non-specific decarboxylases was studied. Complete inhibition of histidine decarboxylation was produced by the alpha-hydrazino analog of histidine (MK 785) a selective inhibitor of the "specific" histidine decarboxylase of rat and mouse tissues\(^{15,17-19}\) (Table 1). In contrast, minimal inhibition of C\(^{14}\)-dopa decarboxylation by MK 785 was observed. When alpha-methyl dopa, a known inhibitor of the "non-specific" decarboxylase, was tested, little inhibition of histi-
LEUKOCYTE HISTIDINE DECARBOXYLASE

Table 2.—Localization of Enzyme Activity Following Leukocyte Separation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Fraction I</th>
<th>Fraction II</th>
</tr>
</thead>
<tbody>
<tr>
<td>L. J.</td>
<td>CML</td>
<td>47.7 cpm/10⁷ cells*</td>
<td>780 cpm/10⁷ cells*</td>
</tr>
<tr>
<td>T. F.</td>
<td>Poly. Vera</td>
<td>190 cpm/10⁷ cells*</td>
<td>863 cpm/10⁷ cells*</td>
</tr>
<tr>
<td>J. H.</td>
<td>Poly. Vera</td>
<td>29.9 cpm/mg. protein†</td>
<td>218.3 cpm/mg. protein†</td>
</tr>
<tr>
<td>A. P.</td>
<td>Secondary Poly.</td>
<td>14.6 cpm/mg. protein†</td>
<td>165 cpm/mg. protein†</td>
</tr>
<tr>
<td>S. R.</td>
<td>Blastic Phase myelofibrosis with myeloid metaplasia</td>
<td>34.2 cpm/mg. protein†</td>
<td>406.6 cpm/mg. protein†</td>
</tr>
</tbody>
</table>

*Whole cell incubations.
†Leukocyte enzyme extract.

decarboxylation was observed, contrasted with complete inhibition of dopa decarboxylation.

Further efforts to distinguish between specific and non-specific decarboxylation involved the addition of various unlabeled substrates to see if decreases in cpm by a substrate dilution effect would occur. When unlabeled L-dopa was introduced into the C¹⁴ histidine incubation, no decrease in cpm was observed. L-tryptophan also failed to depress the yield, while an excess of unlabeled L-histidine, as expected, resulted in decreased counts. When C¹⁴-DL-dopa was employed as substrate, added unlabeled L-histidine was without effect, while unlabeled L-dopa diminished the counts per minute. These data suggest that a specific decarboxylase is responsible for the decarboxylation of histidine demonstrated by the leukocyte enzyme preparation. An L-aromatic amino acid decarboxylase is present as well, but does not appear to decarboxylate histidine to any significant extent.

Enzyme Localization Studies

On the basis of fractionation of leukocytes by centrifugation in albumin solutions of varying specific gravity, it has been estimated that nearly half the total leukocyte histamine is contained within basophils, with the remainder presumed to be confined to other granulocyte types. An effort was made to determine whether cellular localization of histidine decarboxylase coincided with histamine localization. Employing siliconized glass bead columns as well as siliconized nylon wool, mixed leukocyte preparations were separated into two fractions. Fraction I (nonadherent cells) consisted chiefly of lymphocytes and immature granulocytes from myeloblasts through myelocytes, as well as contaminating red cells and platelets, and fraction II (adherent cells) was composed of mature neutrophils, eosinophils, and basophils as well as monocytes. Few monocytes were seen in this fraction when obtained from patients with myeloproliferative disease.

Results are shown in Table 2. In the first two cases, whole cells were incubated, so that differences in intracellular substrate concentration cannot be ruled out. In both cases, decarboxylase activity predominated in fraction II, which consisted of mature granulocytes. In the remaining cases, when leukocyte extracts were assayed, fraction II showed a 7–12-fold increase in activity compared to fraction I.
Table 3.—Effect of Blastic Transformation on Leukocyte Histidine Decarboxylase Activity

<table>
<thead>
<tr>
<th>Date</th>
<th>Blast + Promyelocytes %</th>
<th>Myeloid Cells %</th>
<th>Absolute Basophil Count (Fraction) cells/cu.mm.</th>
<th>Net CPM</th>
<th>CPM mg. total Leuk. prot.</th>
<th>CPM mg. myeloid prot.</th>
<th>CPM/mg Basophil Prot. (× 10⁶)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/14/66</td>
<td>7</td>
<td>84</td>
<td>316</td>
<td>124</td>
<td>56.1</td>
<td>47.7</td>
<td>20.0</td>
</tr>
<tr>
<td>3/3/67</td>
<td>57</td>
<td>36</td>
<td>319</td>
<td>227</td>
<td>25.3</td>
<td>189</td>
<td>16.2</td>
</tr>
<tr>
<td>4/13/67</td>
<td>83</td>
<td>14</td>
<td>175</td>
<td>140</td>
<td>32.5</td>
<td>212</td>
<td>10.8</td>
</tr>
<tr>
<td>4/28/67</td>
<td>6</td>
<td>63</td>
<td>134</td>
<td>190</td>
<td>158.3</td>
<td>250</td>
<td>38.0</td>
</tr>
</tbody>
</table>

Further information on the localization of enzyme in specific cell types has been obtained in patients in whom one particular form of leukocyte predominated in the peripheral blood. Leukocyte extracts prepared from two patients with marked eosinophilia, one, a case of allergic vasculitis with WBC 70,000/cu. mm., 70 percent eosinophils, the other, a patient with "eosinophilic" leukemia, WBC 5,000/cu. mm., 70 percent eosinophils, did not exhibit increased enzyme activity, suggesting that eosinophils do not constitute a particularly rich source of the enzyme. In one patient with chronic lymphocytic leukemia and a leukocytosis of 700,000/cu. mm. with 99 percent small lymphocytes, enzyme activity was normal. An instructive sequence of alterations in enzyme activity occurred in a patient with myelofibrosis and myeloid metaplasia who underwent "blastic" transformation and subsequently responded to chemotherapy. Despite the marked shifts in leukocyte population which occurred during the period of observation, leukocyte histidine decarboxylase activity, in terms of net yield, persisted and remained relatively stable (Table 3). In an attempt to derive information on the type of leukocyte responsible for this continued activity, results were expressed in several ways, in order to detect the cell type whose fluctuations most closely mirrored the alterations in net decarboxylase activity. In these calculations, the assumption is made that the fraction of the total leukocyte protein contributed by each cell type is proportional to the percentage of that cell type in the differential count of the leukocyte preparation. When results were expressed as cpm./mg. total leukocyte protein, a decline in activity was noted in the middle studies. This decline probably reflects the dilution of active leukocyte enzyme protein by relatively inert protein from disrupted myeloblasts and promyelocytes which predominated in the differential count at these times. Enzyme activity was next expressed as "cpm./mg. of myeloid cell protein," the latter term indicating that portion of the total leukocyte protein contributed by more mature myeloid cells (myelocytes through segmented forms), and was calculated by multiplying the total leukocyte protein per ml. by the fraction of myeloid cells in the differential count of the leukocyte concentrate. Results so calculated showed less fluctuation in activity than in the previous expression. In a similar manner, the value for basophil protein was derived by multiplying total leukocyte protein per ml. by the proportion of basophils in the leukocyte concentrate, determined from the absolute basophil count and total leukocyte count. When the cpm per mg. of basophil protein were thus calculated, the activity remained relatively stable and mirrored most closely the fluctuation in net cpm.
Table 4.—Leukocyte Histidine Decarboxylase Activity in Myeloproliferative Disorders

<table>
<thead>
<tr>
<th></th>
<th>Results</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal + Relative Polycythemia</td>
<td>65.7 ± 24.3*</td>
<td>9</td>
</tr>
<tr>
<td>Polycythemia Vera Uncontrolled</td>
<td>80.4 ± 25.3</td>
<td>17</td>
</tr>
<tr>
<td>Polycythemia Vera Controlled</td>
<td>59.6 ± 21.0</td>
<td>5</td>
</tr>
<tr>
<td>Spent Polycythemia Myelofibrosis with Myeloid Metaplasia</td>
<td>98.4 ± 20.0</td>
<td>8</td>
</tr>
<tr>
<td>CML</td>
<td>174.3 ± 56.0</td>
<td>6</td>
</tr>
</tbody>
</table>

*cpm/mg. leukocyte protein/hour ± S.E.

From the above data, both direct and indirect, the following tentative conclusions are drawn: (1) The mature granulocyte appears to be the primary site of histamine formation among peripheral blood leukocytes; (2) the relative contribution of the mature eosinophil, small lymphocyte, and myeloblast to leukocyte histamine formation is minor; and (3) evaluation of the relative contribution of basophils vs. neutrophils to total leukocyte histidine decarboxylase activity must await reproducible methods for the preparation of pure granulocyte subtypes. Centrifugation of mixed leukocytes in albumin and Ficoll of varying concentrations, in our hands, has not proved effective.

Clinical Studies

Table 4 depicts results in patients with myeloproliferative states as well as various control groups. Increased levels of leukocyte histidine decarboxylase activity are seen in uncontrolled polycythemia vera, “spent” polycythemia, and myelofibrosis with myeloid metaplasia, when compared to a control group composed of normal subjects and patients with relative polycythemia. Patients with chronic myelocytic leukemia (CML) also showed increased enzyme activity, the highest levels being seen in three cases with CML. Patients with other hematologic disorders, including chronic lymphatic leukemia (1 case), eosinophilia associated with leukemia (1 case), leukemoid reaction secondary to carcinoma of the pancreas (1 case) and erythrocytosis of unknown etiology (2 cases) demonstrated normal enzyme activity.

Discussion

Prior studies on human leukocyte histidine decarboxylase activity have been limited largely to incubations with intact cells, in which no effort was made to remove endogenous histidine or histamine prior to incubation. Using either whole cells or homogenized ones not subjected to further treatment, it is not possible to control differences in substrate content, which might well affect studies using C¹⁴-histidine as substrate; moreover, differences in the intracellular content of histamine itself might affect
the results. Another uncontrolled factor in whole cell studies includes possible differences in membrane permeability to substrate or cofactor which might influence enzyme activity.23

Despite the shortcomings of whole cell technics, it remains noteworthy that Lindell et al.21 obtained evidence of increased leukocyte histamine formation in patients with polycythemia vera and chronic myelocytic leukemia, and detectable histamine synthesis in five of seven normal subjects. These authors found that blood samples with a high rate of histamine formation had a high content of both basophils and other mature and immature myeloid cells. Although they also noted a significant correlation between “mature” basophils but not “mature” neutrophils or eosinophils, and histamine formation, their evaluation was based on few cases, some of whom had polycythemia vera and who thus would be expected to exhibit a preponderance of both mature and immature myeloid cells other than basophils in their differential count.

The study of leukocyte histidine decarboxylase activity by Hartman, Clark and Cyr22 employed homogenized leukocytes, thus bypassing problems of cell membrane permeability, but made no provision for removal of endogenous substrate. Using this method, they were only able to detect histidine decarboxylase activity in buffy coat preparations from two patients with CML and a marked increase in basophils (49 percent and 77 percent basophils, respectively), but not in leukocyte preparations from a case of chronic lymphatic leukemia, two cases of acute myeloblastic leukemia, and three cases of secondary eosinophilia. The insensitivity of their method thus prevented the evaluation of the histidine decarboxylase activity of leukocytes other than basophils.

By eliminating problems of cell permeability, variations in endogenous substrate content, and the possible inhibitory effects of endogenous histamine, our procedure for the assay of leukocyte histidine decarboxylase has permitted the detection of this enzyme in the leukocytes of all subjects studied, and has allowed its characterization with respect to substrate specificity and kinetic properties. The enzyme appears to be localized to granulocytes which have matured beyond the promyelocyte stage.

In the clinical studies, it has been possible to demonstrate increased enzyme activity in those patients with myeloproliferative disorders in whom elevated leukocyte and/or urine histamine levels occur, i.e., uncontrolled polycythemia vera, spent polycythemia, myelofibrosis with myeloid metaplasia, and chronic myelocytic leukemia. This increased enzyme activity would appear to represent a true increase in histamine-forming capacity per myeloid cell, rather than an apparent increase as a result of the increased percentages of myeloid cells seen in these cases. When enzyme activity is expressed as cpm./mg. of myeloid cell protein, thus correcting for variations in the differential count, the differences in enzyme activity between normal and myeloproliferative subjects remain. Moreover, the normal enzyme activity in leukemoid reaction provides further evidence for increased enzyme activity per myeloid cell in myeloproliferative disorders.

The present study has not solved the problem of the contribution of the
basophil to total leukocyte histamine formation in myeloproliferative disease. While a rough correlation has been observed between elevated absolute basophil count and increased leukocyte histamine content,\textsuperscript{3} discrepancies occur in which leukocyte histamine is elevated in myeloproliferative cases in the presence of a normal basophil count, and vice versa. A recent study\textsuperscript{24} has presented evidence that in CML, histamine content per basophil is actually diminished. The present study includes two cases of CML with marked granulocytosis and a striking increase in the absolute basophil count, but with normal levels of leukocyte histamine and histidine decarboxylase activity, while these latter parameters were elevated in other cases of CML with similar hematologic findings. The relative contribution of the various granulocyte subtypes to leukocyte histidine decarboxylase activity will be properly assessed only with the development of reliable methods for obtaining adequate numbers of pure subtypes.

The increased leukocyte enzyme activity demonstrated in myeloproliferative disorders may be merely quantitative, reflecting an alteration in the mechanisms regulating intracellular enzyme levels so that increased levels of “normal” enzyme result. Alternatively, the enzyme protein itself, being produced by a neoplastic cell, may be abnormal. Information on this point must await the outcome of current efforts to identify possible isozymes of histidine decarboxylase after starch gel electrophoresis of leukocyte extracts, and to purify the enzyme using ammonium sulfate fractionation\textsuperscript{17} combined with DEAE cellulose chromatography.

**Summary**

1. Histidine decarboxylase was assayed in extracts from human leukocytes and the properties of the enzyme studied.

2. Leukocyte histidine decarboxylase was found to be substrate-specific, to require pyridoxal phosphate as co-enzyme, and to be inhibited by alpha-hydrazino analog of histidine (MK 785), a selective inhibitor of the specific histidine decarboxylase occurring in rat tissue. A non-specific L-aromatic amino acid decarboxylase was also demonstrated in leukocyte extracts, which possessed little activity toward histidine.

3. Cellular localization studies revealed that mature neutrophils and basophils possessed most of the histidine decarboxylase activity exhibited by mixed leukocyte preparations. Mature eosinophils, small lymphocytes, and immature myeloid cells (myeloblasts and promyelocytes) showed little histidine decarboxylase activity.

4. In the clinical studies, patients with uncontrolled polycythemia vera, “spent” polycythemia, myelofibrosis with myeloid metaplasia, and chronic myelocytic leukemia, showed increased leukocyte enzyme activity when compared to a control group composed of normal subjects and patients with relative polycythemia. This increased activity appears to represent a true increase in enzyme activity per granulocyte, and is believed to account for the elevated leukocyte histamine content demonstrated in patients with myeloproliferative disorders.
SUMMARIO IN INTERLINGUA
1. Decarboxylase de histidina esseva estimate in extractos ab leucocytos human, e le proprietates del enzyma esseva studiate.
2. Esseva trovate que decarboxylase de histidina ab leucocytos es substrato-specific, require phosphato pyridoxalic como co-enzyma, e pote esser inhibite per le analogo alpha-hydrazinic de histidina (MK 785), le qual es un inhibitor specific del decarboxylase de histidina que occurre in tissu de rattos. Un non-specific decarboxylase de amino-acido L-aromatic esseva etiam demonstrate in extractos leucocytic. Isto manifestava pauc activitate verso histidina.
3. Studios de localisation intracellular revelava que matur neutrophilos e basophilos possedeva le plus grande parte del activitate de decarboxylase de histidina presente in mixte preparatos de leucocytos. Matur eosinophilos, micre lymphocytos, e immatur cellulas myeloide (myeloblastos e promyelocytos) monstava pauc activitate de decarboxylase de histidina.
4. In le studios clinic, patientes con non-stabilisate polycythemia ver, polycythemia "exhaurite," melofibrosis con metaplasia myeloide, e chronic leucemia myelocytic manifestava augmentate activitate enzymatic in leucocytos in comparation con un gruppo de controlo componite de subjectos normal e de patientes con polycythemia relative. Iste augmentate activitate pare representar un ver augmento in le activitate per granulocyto individual. Es supponite que illo explica le elevate contento leucocytic de histamina que ha esite demonstrate in patientes con disordines myeloproliferative.

REFERENCES


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