On the Identification of Octopamine in Mammals*

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Many of the phenolic acids in human urine have been characterized, and several have been tentatively identified by means of their behavior on paper chromatograms (3). Further studies have revealed that most of them originate from dietary precursors, but a few have been found to be excreted always and in amounts which are relatively constant for a given individual despite marked changes in the diet. Among these are 4-hydroxy-3-methoxymandelic acid, homovanillic acid, 5-hydroxyindoleacetic acid, and another acid which was identified tentatively as p-hydroxymandelic acid (3). The first three acids cited are known to be metabolites of the catecholamines and of serotonin, and monoamine oxidase is known to be involved in their metabolism.† By analogy, it seemed likely that p-hydroxymandelic acid might be a metabolite of the corresponding amine, p-hydroxymandelamine. The occurrence of this amine in nature was reported in 1952 by Erspamer (4), who identified it in extracts of salivary glands of the octopus and named it octopamine. Erspamer and his colleagues were not able to detect octopamine in other tissues of the octopus or in extracts from the tissues of vertebrates or invertebrates (5).

With the use of ion exchange resins to separate selectively and to concentrate very small amounts of amines for two-dimensional paper chromatography, and with the use of inhibitors of monoamine oxidase to prevent the destruction of octopamine, it has been possible to demonstrate its presence in various tissues of the rabbit. In addition, it has been found to occur in the urine of humans, rats, and rabbits treated with monoa mine oxidase inhibitors, and in very much smaller amounts in their normal urine. The large proportionate increase in octopamine in animals treated with monoamine oxidase inhibitors is suggestive that octopamine may be an important amine for consideration in studies on the therapeutic effects of the inhibitors.

EXPERIMENTAL PROCEDURE AND RESULTS

p-Hydroxymandelic Acid—The tentative identification of HMA* in urine was based upon its Rf values in several solvent systems and its color reactions with diazotized p-nitroaniline and diazotized sulfanilic acid (3). More than 2000 samples of normal and pathological urine have been examined without the finding of a grossly elevated excretion of HMA. The small amount in urine made definitive identification of the compound by isolation seem impractical, and paper chromatographic techniques were used to make certain its identity.

An amount of urine which contained 100 mg of creatinine was acidic to pH 1 and extracted with ethyl acetate; the solvent was removed in a vacuum, and the residue was taken up in a small amount of ethanol and applied to 20 sheets of Whatman 3 MM paper. Two-dimensional paper chromatography was carried out on each sheet with isopropyl alcohol-aqueous ammonia-water (8:1:1) as the first solvent system and benzene-propionic acid-water (10:9:1) as the second. The appropriate area on each sheet was marked under ultraviolet light and cut out, and the HMA was eluted with ethanol. Amounts of the eluate which contained approximately 1 to 2 µg of HMA and corresponding amounts of authentic HMA were run on paper chromatograms in five solvent systems, in which their mobilities were found to be identical. The results are shown in Table I. The qualitative tests, also listed in Table I, were the same for urinary and authentic compounds, and the color yields with each were comparable. The red color with diazotized p-nitroaniline, yellow with diazotized sulfanilic acid, and blue with Gibbs’ reagent indicated the presence of a phenolic group, the periodate-benzidine reaction showed an α-hydroxy acid grouping.

An amount of eluate which contained approximately 100 µg of HMA was reduced by refluxing it overnight with 1 ml of hydroxyl acid and 5 mg of red phosphorus. Hydroxyl acid was removed in a vacuum, and residual iodine was removed by adsorption on charcoal. Authentic HMA was treated in the same manner. Almost quantitative formation of p-hydroxyphenylacetic acid from both compounds was demonstrated by paper chromatography with the solvent systems and qualitative reactions shown in Table I.

Finally, a sample of eluate which contained approximately 100 µg of HMA was converted to p-hydroxybenzaldehyde by dissolving it in 0.02 ml of acetic acid and 0.08 ml of 0.5% KI, and letting the solution stand at room temperature for 20 hours. The identity of the p-hydroxybenzaldehyde from the urinary HMA was demonstrated by comparison of its chromatographic properties with those of authentic aldehyde, as shown in Table I. The agreement between the properties of the urine compound and its derivatives and those of the authentic compounds provides reasonable assurance of the identity of the urine metabolite.

Free HMA is present in rabbit, rat, and cat urine in approximately the same amount as in human urine. No evidence for

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‡ p-Hydroxymandelamine has been referred to as octopamine, noroctopamine, noroctympathol, and p hydroxy a (aminomethyl) benzyl alcohol. It had been known as a pharmaceutical product benzyl alcohol. It had been known as a pharmaceutical product

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the presence of any conjugated acid was obtained in the human, rabbit, or cat urine, but rat urine contains some bound HMA. The amount of HMA in most samples of human urine ranges from approximately 0.6 to 2.5 μg per mg of creatinine, which corresponds to an excretion of 1 to 4 mg daily for an average adult.

Identification of Octopamine in Urine from Iproniazid-treated Rabbits—In order to provide a sufficient supply of tissues for later work, rabbits were selected as experimental animals. Because of the very small quantities of amines ordinarily present in urine, a monoamine oxidase inhibitor was used to increase the amount so that enough material could be accumulated for identification studies. Three male rabbits (New Zealand White) were treated with intramuscular injections of iproniazid (1-isonicotinoyl-2-isopropylhydrazine), 150 mg per kg of body weight, in urine, a monoamine oxidase inhibitor was used to increase the amount so that enough material could be accumulated for later work, rabbits were selected as experimental animals. Be-

<table>
<thead>
<tr>
<th>Table I: Rf values and color reactions of octopamine and related compounds</th>
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<tbody>
<tr>
<td>Isopropyl alcohol-aqueous ammonia-water (8:1:1)</td>
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<tr>
<td>n-Butanol-acetic acid-water (4:1:1)</td>
</tr>
<tr>
<td>Benzene-propionic acid-water (10:9:1)</td>
</tr>
<tr>
<td>Benzene-propionic acid-water (10:18:5)</td>
</tr>
<tr>
<td>Aqueous KCl (20%)</td>
</tr>
<tr>
<td>Diazotized p-nitroaniline (6)</td>
</tr>
<tr>
<td>Diazotized sulfanilic acid (7)</td>
</tr>
<tr>
<td>Gibbs' reagent (8)</td>
</tr>
<tr>
<td>KI-reagent*</td>
</tr>
<tr>
<td>Indophenolic acid (9) or 2,4- dinitrophenyl-hydrazine (10)</td>
</tr>
</tbody>
</table>

* The chromatograms are sprayed with 0.01 M KI04, allowed to stand 10 minutes, and then sprayed with a 0.2% solution of benzidine in 0.05 N HCl in 50% aqueous ethanol. Faint yellow or white spots on a blue background indicate positive reactions.

In order to identify conclusively the urine amine as octopamine, it was subjected to further purification. The extract was streaked on ten sheets of Whatman 3 MM paper, and chromatography was carried out in isopropyl alcohol-aqueous ammonia-water (8:1:1). The area of the paper which contained the octopamine was cut out, the substance was eluted with 70% ethanol, and the eluate was concentrated, dissolved in 2 ml of 0.2 N ammonium acetate, pH 6.0, and subjected to chromatography on a column (2 x 95 cm) of Amberlite IRC-50 according to the method of Kirshner and Goodall (13); 4-ml fractions were collected. Authentic octopamine was located in the eluate by measurement of its absorption at 272 mμ and by paper chromatography of a portion of each fraction; it was found to emerge in the fraction between 592 and 720 ml. The portion of the urine extract which emerged in this fraction was desalted by passing the acidified solution through a column of Dowex 50 (H⁺) and eluting the adsorbed substance with aqueous ammoniacal ethanol. This eluate was concentrated to dryness in a vacuum, and the residue, which contained approximately 400 μg of octopamine along with a small amount of normetanephrine, was taken up in 2 ml of 0.2 N phosphate buffer, pH 8.65. The octopamine was freed from normetanephrine by chromatography on a column (1 x 90 cm) of Amberlite IRC-50, (200 to 400 mesh), which had been conditioned with 0.2 N phosphate buffer, pH 8.65. The elution patterns of urinary and authentic octopamine with this buffer are shown in Fig. 1. The middle fraction of the octopamine peak was used for determination of ultraviolet absorption spectra and fluorescence and activation spectra, which are shown in Figs. 2 to 4. These properties of authentic and urinary octopamine were essentially identical at both acid and alkaline pH values.

The entire fraction which emerged from 234 to 264 ml was desalted and used for further studies. Isolated and synthetic octopamine had the same Rf values in five solvent systems and the same qualitative reactions, as shown in Table I; the color yields with the different reagents were comparable for the two materials. These included the characteristic reactions of a phenol: yellow color with diazotized sulfanilic acid, pink with
I gave a red color with diazotized p-nitroaniline and yellow with diazotized sulfanilic acid, and showed no reaction with ninhydrin.

Finally, an amount of extract containing 100 μg of octopamine was subjected to enzymatic oxidation by a preparation made by homogenizing rabbit liver with 2 volumes of cold 0.1 N phosphate buffer, pH 7.4, followed by centrifugation for 20 minutes at 1000 × g. The octopamine was added to 1 ml of the supernatant solution, and incubation was carried out at 37° for 2 hours in an open flask in a Dubnoff metabolic shaker. The digest was acidified to pH 1 with concentrated HCl and shaken with ethyl acetate, acids were extracted from the solvent into

diazotized p-nitroaniline, and sky-blue with Gibbs' reagent; an amine as shown by a gray color with ninhydrin; and an adjacent hydroxyamine group, indicated by the periodate-benzidine reaction.

A volume of the isolated material which contained approximately 100 μg of octopamine was oxidized with KIO₄ in the manner described for the oxidation of HMA. Quantitative formation of p-hydroxybenzaldehyde was demonstrated with paper chromatography in the solvent systems and with the reagents listed in Table I.

Acetylation provided another derivative. An amount of solution containing 100 μg of isolated octopamine was concentrated to dryness, the residue was dissolved in 1 ml of saturated sodium bicarbonate solution, and the amine was acetylated by the addition of 0.5 ml of acetic anhydride at room temperature. The acetylated amine was extracted from the acidified solution into 5 ml of methylene dichloride. Authentic octopamine was acetylated in the same manner. Both extracts contained a substance which had the same R_f values in five solvent systems,

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FIG. 1. Elution patterns of purified urinary amines and authentic octopamine with 0.2 N phosphate buffer, pH 8.65, from a column (1 × 90 cm) of Amberlite IRC-50. Dashed line, authentic octopamine; solid line, urine amines.

FIG. 2. Absorption spectra of octopamine in 0.2 N phosphate diazotized p-nitroaniline, and sky-blue with Gibbs' reagent; an amine as shown by a gray color with ninhydrin; and an adjacent hydroxyamine group, indicated by the periodate-benzidine reaction.

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10% sodium bicarbonate, the bicarbonate solution was acidified, and the phenolic acids were extracted back into ethyl acetate. Paper chromatography, as described earlier, showed the presence of p-hydroxymandelic acid in the concentrated extract. No phenolic acids were found when liver extract alone was treated in the same manner. Formation of HMA from the isolated octopamine by the preparation, which contains monoamine oxidase and aldehyde dehydrogenase activity (14), provided additional evidence for the identity of octopamine.

The above experiments for the identification of octopamine were repeated on material isolated by a modified procedure from a smaller amount of urine from iproniazid-treated rabbits. The amines in an amount of urine containing 300 mg of creatinine were concentrated with Dowex 50 and were then chromatographed on Amberlite IRC-50 at pH 8.65. In this system, octopamine emerges with p-tyramine, which was separated from octopamine by subsequent chromatography on Amberlite IRC-50 at pH 5.0. The fraction from the middle of the octopamine peak showed absorption and fluorescence spectra identical with those of authentic octopamine at pH 5 and 9.8; the amount present was estimated to be approximately 200 μg.

Rabbits were treated by injection with 10 mg per kg of body weight of another type of monoamine oxidase inhibitor, β-phenylisopropylhydrazine (JB 516), and urine was collected for the next 4 days. The amines in an amount of urine containing 10 mg of creatinine were concentrated on Dowex 50 and eluted, and the entire sample was subjected to two-dimensional paper chromatography. The substance which has the Rp values and qualitative reaction of octopamine was detected in an amount estimated to be 0.5 μg per mg of creatinine.

With this procedure, albino rats (Sprague-Dawley strain) maintained on a synthetic diet were found to excrete 0.01 to 0.03 μg of octopamine per mg of creatinine. After injection with iproniazid (100 mg per kg of body weight) the excretion increased to 0.3 μg per mg of creatinine.

In order to test octopamine in the urine of undrugged rabbits and humans, it was necessary to use a much larger amount of urine and to effect a more extensive purification of the amine fraction in order to remove materials which interfered with the paper chromatography of the amines. This was done by concentrating the amines with Dowex 50 as usual, and then chromatographing the concentrate on a column (1 × 90 cm) of Amberlite IRC-50 at pH 8.65 before paper chromatography. In this manner it was possible to detect octopamine in an amount estimated to be 0.5 μg per mg of creatinine in human urine and 1 μg per mg of creatinine in rabbit urine.

Identification of Octopamine in Organs of Rabbits Treated with Monoamine Oxidase Inhibitors—Four rabbits were injected twice with 100 mg of iproniazid per kg of body weight at 24-hour intervals and were killed 24 hours after the last injection. The brains, kidneys, and spleens were dissected immediately. The total weights of the organs were as follows: hearts, 27.2 g; kidneys, 80.9 g; and spleens, 8.5 g. The pooled organs were homogenized immediately in 500 ml of 80% ethanol, 0.3% in sulfuric acid. The homogenate was allowed to stand 2 hours at room temperature; then it was centrifuged, and the supernatant fluid was separated. The precipitate was suspended in another 300 ml of the acidic aqueous ethanol for 2 hours, and the additional supernatant fluid was separated and combined with the first. The pH was adjusted to 5 by the addition of 2 N NaOH, and the resulting solution was passed through a column (2 × 20 cm) of Dowex 50 (H+) which had previously been suspended in 10% ethanol. The resin was washed successively with 300 ml of 70% ethanol, 300 ml of 0.1 N sodium acetate, and 150 ml of water, and the adsorbed amines were eluted with 150 ml of ammoniacal ethanol. The eluate was concentrated to dryness in a vacuum, and the residue was dissolved in 2 ml of 0.2 N phosphate buffer, pH 8.65. This solution was applied to a column (1 × 90 cm) of Amberite IRC-50 which had been conditioned with the same buffer. Upon chromatography with this buffer, an estimated 80 μg of octopamine, contaminated with p-tyramine, emerged in the eluate fractions from 236 to 286 ml. This fraction was desalted and concentrated, and the residue was dissolved in 1 ml of 0.4 N ammonium acetate buffer, pH 6.0, and subjected to chromatography on a column (1 × 40 cm) of Amberite IRC-50 as described by Kirshner and Goodall (13). Octopamine emerged between 128 and 152 ml. The middle 4-ml fraction was used for measuring the ultraviolet absorption and fluorescence and activation spectra, which were identical with those of authentic octopamine at pH 5 and 9.8. The total fraction was subjected to the same tests for identification described for the urinary compound, with the same results, except that the purified extract from organs contained a small amount of ninhydrin-positive substances and a material which gave a faint yellow color with the periodate-benzidine reaction.

In order to estimate the amount of octopamine in the organs of the rabbits, the acid ethanol extract was passed through a column of Dowex 50 as described above, and the eluate was purified by chromatography on a column (1 × 20 cm) of Amberlite IRC-50 at pH 8.65. Aliquots of the desalted eluate from this column were subjected to two-dimensional paper chromatography as described earlier. The amounts of octopamine and normetanephrine on the chromatograms were estimated by visual comparison with the spots produced by chromatography of known amounts of authentic compounds on the same chromatograms. Recovery of octopamine added to tissues which were then processed in the same manner was 70%. Aliquots of the original acid ethanol extract were assayed fluorimetrically for norepinephrine and serotonin with the methods of von Euler and Lisjajko (15) and Bogdanski et al. (16), respectively. The results, which allow a comparison of the change in the levels of these four amines, are presented in Table II.

Effect of Iproniazid Treatment on Excretion of Octopamine and HMA in Rat—Three 300-g male albino rats were maintained on a synthetic diet (17). After 5 days their urine was collected and pooled for a 4-day period. Each animal was then treated by
two intraperitoneal injections (100 mg per kg each) of iproniazid on 2 successive days, and urine was collected for 4 days, beginning at the time of the first injection. The amount of free and conjugated HMA and octopamine was estimated chromatographically; after the free acid or amine had been removed, the conjugated forms were released by treatment with Glusulase (Endo-Products, Inc.). Less than 0.1 µg of free or conjugated octopamine per mg of creatinine was present before iproniazid treatment, and 0.8 and 0.3 µg per mg of creatinine, respectively, afterward. Before treatment, 12 µg of free HMA and 5 µg of conjugated HMA were excreted per mg of creatinine; after treatment, these levels fell to 5 and 3 µg of HMA per mg of creatinine, respectively. The decrease in HMA excretion could not be accounted for by the increased excretion of octopamine. This might occur because of an accumulation of amines in the body or, more probably, as a result of the metabolism of octopamine through some pathway other than by the action of monoamine oxidase.

DISCUSSION

The older literature contains a report that large amounts of p-hydroxyxymandelic acid are excreted by patients with acute yellow atrophy of the liver (18), but later works demonstrated that the material observed actually was p-hydroxyphenylacetic acid (19). In the present paper, the previous chromatographic identification of p-hydroxyxymandelic acid has been strengthened by the demonstration that hydriodic acid reduction converted it to p-hydroxyphenylacetic acid, and periodic acid oxidation, to p-hydroxybenzaldehyde. These experiments provide convincing evidence for the identity of the urine metabolite.

The hypothesis that HMA may be the end product of octopamine metabolism was substantiated by the positive identification of octopamine in the urine and tissues of animals treated with monoamine oxidase inhibitors. In order to eliminate the possibility that octopamine might have been formed as a specific response to treatment with iproniazid, another inhibitor with a different type of structure, β-phenylisopropylhydrazine (JB 516), was also used with the same resulting accumulation of octopamine. More direct evidence that octopamine is the precursor of urinary HMA was provided by experiments with rats, in which a decreased excretion of HMA was observed when the animals were treated with iproniazid.

Despite the fact that the amount of HMA in urine is approximately the same as the 4-hydroxy-3-methoxymandelic acid produced from epinephrine and norepinephrine and the 5-hydroxyindoleacetic acid produced from serotonin, octopamine could never be detected in tissue extracts from undrugged animals. A concentration comparable to that of norepinephrine or serotonin would have been easily measured. The low concentration actually present must reflect a very high turnover rate for octopamine. No conjugates of octopamine or of HMA could be detected in any species except the rat. The much greater relative increase in octopamine than in norepinephrine and serotonin in the tissues of monoamine oxidase-treated animals is perhaps indicative that inactivation by monoamine oxidase is a more important pathway for octopamine than for the other amines.

The manner of origin, the tissue or type of cell in which it is formed, and possible physiological functions of octopamine are at the present time obscure. Recently it was reported that dopamine β-oxidase, the enzyme activity of brain and adrenal tissue which converts dopamine to norepinephrine, is able to accept p-tyramine to octopamine. Adrenal tissue was found to be far more active than any other for this reaction (20). The fact that an increased excretion of HMA has never been observed in patients with phaeochromocytoma, sympathoblastomas, or neuroblastomas who excrete greatly increased amounts of 4-hydroxy-3-methoxymandelic acid, the end product of epinephrine and norepinephrine metabolism, argues against the adrenals or sympathetic nerve tissues as a major site of formation of octopamine and HMA. In this work, attempts to detect octopamine in the adrenals of the iproniazid-treated rabbits were unsuccessful, although a level of 1 µg per g of tissue would have been readily measurable. A similar attempt with the aortic and inferior vena cava tissue from the same animals was unsuccessful; 0.1 µg per g would have been detectable in this case.

Thus, it was not possible to locate any tissue of the iproniazid-treated rabbit which appeared to have a singular ability to synthesize octopamine in a manner analogous to the formation of serotonin by the intestine or epinephrine and norepinephrine by the adrenals. The finding in heart and kidney of a very large proportionate increase and the highest actual levels observed in iproniazid-treated animals conceivably could point to an important physiological function of octopamine in these organs. In the heart, a large amount of octopamine and a trace of normetanephrine were the only phenolic amines which could be detected on paper chromatograms; in the kidney, a small amount of p-tyramine was also present. It is possible that the beneficial effects of monoamine oxidase inhibitors in the treatment of anginal pain might result from the accumulation of octopamine. Unfortunately, detailed studies on the pharmacology of octopamine are not available.

After the heart and kidney, the brain had the highest concentration of octopamine, although normetanephrine, methoxytyramine, and p-tyramine were also prominent on paper chromatograms. In analogy with the localization of norepinephrine, dopamine, and serotonin in specific areas of the brain, a similar local high concentration of octopamine could exist. In such case the concentration of octopamine in localized areas of the brain could well be higher than in any other tissue of the body.

In the past there was a tendency to ascribe clinical effects of the monoamine oxidase inhibitors to an increased level of norepinephrine and serotonin in tissues. More recently, the finding that dopamine, p-tyramine, and tryptamine are normal metabolites has made it necessary to consider the possible physiological effects of increased levels of these and perhaps other amines. The present work makes it apparent that octopamine should receive special attention in connection with physiological effects of monoamine oxidase inhibitors because of its rapid destruction in vivo and the fact that the proportionate increase in tissue levels after monoamine oxidase blockade is far greater than that of any other of the amines.

SUMMARY

1. Evidence has been presented to confirm the identity of p-hydroxyxymandelic acid, which is present as a constant constituent of human urine.

2. Octopamine (norsympathol, p-hydroxyxymandelamine) has been positively identified in the urine and in tissue extracts of rabbits treated with monoamine oxidase inhibitors. Its presence has been demonstrated also in urine from normal rats, rabbits, and humans.
3. The occurrence of octopamine in mammals and its possible significance have been discussed.

REFERENCES
2. ARMSTRONG, M. D., AND KAKIMOTO, Y., Abstr. 1st International Congress of Endocrinology (Copenhagen), 1960, p. 1037.
On the Identification of Octopamine in Mammals
Yasuo Kakimoto and Marvin D. Armstrong


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