Isolation of a Tridecapeptide from Bovine Intestinal Tissue and its Partial Characterization as Neurotensin*

(Received for publication, June 14, 1976)

PATRICK KITABGI, ROBERT CARRAWAY, and SUSAN E. LEEMAN

From the Department of Physiology and Laboratory of Human Reproduction and Reproductive Biology, Harvard Medical School, Boston, Massachusetts 02115

Radioimmunoassayable neurotensin (R-NT) has been isolated from acid/acetone extracts of 50 kg of calf small intestine with an overall yield of approximately 15%. The concentration of R-NT in calf intestinal tissue was approximately 35 pmol/g wet weight. Throughout the purification procedures which involved adsorption onto sulfopropyl (SP)-Sephadex, chromatography on Sephadex G-25 and SP-Sephadex, immunoadsorption on neurotensin-antibody Sepharose and high voltage paper electrophoresis, R-NT displayed the chromatographic and electrophoretic properties of neurotensin. R-NT was found to contain a tridecapeptide with the same amino acid composition as neurotensin. This peptide yielded the same products as neurotensin when submitted to digestion by carboxypeptidase A or papain. Its immunological properties were indistinguishable from those of neurotensin and its potency in stimulating hypotension in anesthetized rats was comparable to that of synthetic neurotensin. If the amino acid sequence of this peptide proves to be the same as that of neurotensin, then neurotensin is another biologically active peptide isolated from both brain and intestinal tissues.

Recently, the discovery of a vasoactive peptide, neurotensin, and its isolation from bovine hypothalami were reported by Carraway and Leeman (1). Subsequently, the sequence of neurotensin was shown to be Glu-Leu-Tyr-Glu-Asn-Lys-Pro-Arg-Arg-Pro-Tyr-Ile-Leu-OH (2) and when a peptide was synthesized according to this sequence it was found to be chemically and biologically indistinguishable from the native material (3). The availability of synthetic material made it possible the development of a radioimmunoassay for neurotensin (4, 5). Using this radioimmunoassay, radioimmunoassayable neurotensin (R-NT) was found not only to have a differential distribution throughout brain (6) but was also present in extracts of small intestinal tissue in approximately the same concentrations as in hypothalamic tissue. Therefore, it seemed feasible as well as of considerable interest to isolate and characterize this material in order to determine if the R-NT was neurotensin itself or a different but closely related peptide.

Experimental Procedures

Materials

Bovine small intestinal tissue extending from the duodenum to the ileum was obtained at a local slaughter house. The tissue was dissected within 15 min after death, gently washed, and frozen immediately in a dry ice/acetone mixture. Albino rats were obtained from Charles River Breeding Laboratory. Sephadex gel and CNBr-activated Sepharose 4B were obtained from Pharmacia Chemical Co., and chromatography paper from Whatman. Synthetic neurotensin was obtained from Beckman, Bioproducts Division. Neurotensin as well as neurotensin antiserum (poly(Glu6', Lys4')-6 and poly(Glu4', Lys6')-4) obtained in rabbit, were prepared in the laboratory as previously described (5). Carboxypeptidase A and papain were as previously reported (1). Sodium pentobarbital (Nembutal) was obtained from Abbott Laboratories. All reagents were reagent grade from Fisher Chemical Co.

Methods

Analytical Procedures

Gel Chromatography Ion Exchange Chromatography and High Voltage Paper Electrophoresis—Chromatography on Sephadex G-25 or sulfopropyl Sephadex G-25, as well as high voltage paper electrophoresis were done as described by Carraway and Leeman (1) for the isolation of neurotensin from bovine hypothalami. Protein concentration of column eluates were measured by their absorbance at 280 nm, assuming that 1 absorbance unit represented 1 mg/ml of protein.

Amino Acid Analysis—All amino acid analyses were performed on a Beckman model 121 M Automatic Amino Acid Analyzer. Samples of peptides (1 to 2 nmol) were hydrolyzed with 0.2 ml of 6 N HCl 10\(^{-3}\) M phenol in evacuated, sealed tubes at 109\(^{\circ}\)C for 24 to 72 h.

Radioimmunoassay—During the course of its purification, the intestinal R-NT was detected using the radioimmunoassay for neurotensin described previously (4). Two rabbit antibodies generated against neurotensin, poly(Glu'6', Lys'4')-6 and poly(Glu'6', Lys'4')-4, were used...
in the assay: poly(Glu^{6}, Lys^{4})-4 recognized the COOH-terminal region of neurotensin, while poly(Glu^{8}, Lys^{4})-6 appears to require the entire sequence of neurotensin to be fully active (5). Partial sequences, thus possible degradation products of neurotensin possessing the COOH-terminal sequence of the molecule cross-react with poly(Glu^{6}, Lys^{4})-4, while they show very little, if any, activity with poly(Glu^{8}, Lys^{4})-6. Therefore, the ratio of poly(Glu^{6}, Lys^{4})-4 over poly(Glu^{8}, Lys^{4})-6 measurement of R-NT was considered to be a good indication of the integrity of the material throughout the purification procedure.

Affinity Chromatography—Sepharose 4B actuated with CNBr was coupled to purified poly(Glu^{6}, Lys^{4})-4 neurotensin antisera as described by Carraway and Leeman (5). The binding capacity of the immunosorbent used in this work was about 200 nmol when tested with synthetic neurotensin.

Enzymatic Procedures—Enzymatic digestions by carboxypeptidase A and papain were done as previously described (2). Amino acids released by the action of carboxypeptidase A were detected on the amino acid analyzer. Papain-generated fragments of neurotensin and intestinal material were separated by high voltage paper electrophoresis at pH 6.5.

Biological Procedure—Systemic blood pressure was measured with a Hewlett Packard recorder and pressure transducer following cannulation of the carotid artery in rats weighing 250 to 300 g and anesthetized with pentobarbital (50 mg/kg).

**Isolation Procedure**

Extraction of Tissues—The frozen tissue (about 50 kg) was homogenized with an equal volume (50 liters) of acetone, 1 N HCl (100/3, v/v) in a Gilford Wood colloid mill, then 3 more volumes of this solvent were added, and the suspension was stirred. The mixture was suction-filtered through Whatman No. 31 paper on Buchner funnels. The filtrate was mixed with 200 liters of petroleum ether in order to remove lipids as well as acetone. The ether/acetone phase was discarded and the process repeated with 200 liters of petroleum ether. The acetone/water phase (80 liters at this stage) was then evaporated under reduced pressure at room temperature to a final volume of 35 liters.

Absorption on SP-Sephadex—The aqueous phase was diluted to 200 liters with distilled water and the pH adjusted to 5.0 with acetic acid. SP-Sephadex (300 g) previously swollen in 0.1 M acetic acid was added to the 200-liter solution and stirred overnight at 4°C. After decanting and filtrating the solution, the gel was washed with 10 liters of 0.1 M acetic acid and eluted with 2 liters of 1 M pyridine/acetate, pH 5.5.

First Chromatography on Sephadex G-25—Of the pyridine acetate eluate, 1 liter was applied to a 20-liter column of Sephadex G-25 (fine) equilibrated in 0.1 M acetic acid at 4°C. The immunoreactive material eluted from the column was detected by radioimmunoassay (Fig. 1). The remaining liter of the pyridine/acetate eluates was chromatographed in the same condition and the immunoreactive regions of the two columns were pooled (5.5 liters). The initial extraction and the purification steps thus far were performed at the New England Enzyme Center, Tufts University, School of Medicine, Boston, Mass.

First Cation Exchange Chromatography—This pool was then applied at room temperature to a 100-ml column of sulfoethyl Sephadex C-25 equilibrated with 0.1 M acetic acid. The column was eluted with a linear gradient ranging from 0.05 M pyridine/acetate, pH 3.1, to 1 M pyridine/acetate, pH 5.5. The active region was located by radioimmunoassay (Fig. 2) and pooled. The volume of the pool (370 ml) was reduced to 100 ml by lyophilization.

Second Chromatography on Sephadex G-25—The 100-ml pool was applied to a 5-liter column of Sephadex G-25 (fine) equilibrated in 0.1 M acetic acid. The fractions were examined for R-NT (Fig. 3). The active fractions were pooled and the pool lyophilized.

Affinity Chromatography—The lyophilized material was taken up in 150 ml of 0.05 M phosphate buffer, pH 7.4. This solution was treated in three separated batches of 50 ml each (in order not to exceed the capacity of the antibody-Sepharose conjugate) using the following procedure: 90 ml of the solution were incubated for 24 h at 4°C with the antibody-Sepharose conjugate. After incubation, the mixture was filtered on a Buchner funnel. The filtrate was put aside. The gel was

![Fig. 1. Gel chromatography of bovine intestinal extract on Sephadex G-25. Sample in 1 M pyridine/acetate (1 liter) represents half of the material obtained after SP-Sephadex extraction in Table I; column size, 14 x 150 cm (resin volume 201); fraction size, 400 ml; eluent, 0.1 M acetic acid; flow rate, 10 ml/min. Immunoreactivity was measured by radioimmunoassay using poly(Glu^{6}, Lys^{4})(PGL)-6 (■) and poly(Glu^{8}, Lys^{4})-4 (■) antibodies. Similar results were obtained when the other half of the material was chromatographed on the same conditions.](https://example.com/fig1)

![Fig. 2. Ion exchange chromatography on sulfoethyl Sephadex C-25. Sample represents the material obtained from Fractions 23 to 28 of the two columns in Fig. 1; resin volume 100 ml; fraction size, 90 ml; column eluent, pyridine/acetate, 0.05 M (pH 3.1) to 1 M (pH 5.5). Immunoreactivity was measured by radioimmunoassay using poly(Glu^{6}, Lys^{4})(PGL)-6 (■) and poly(Glu^{8}, Lys^{4})-4 (■) antibodies.—, an estimate of the pH gradient.](https://example.com/fig2)

![Fig. 3. Rechromatography of neurotensin-like immunoreactivity on Sephadex G-25. Sample represents Fractions 27 to 42 in Fig. 2; column size, 8 x 100 cm (resin volume 5 liters); fraction size, 23 ml; eluent, 0.1 M acetic acid; flow rate, 4 ml/min. Immunoreactivity was measured by radioimmunoassay using poly(Glu^{6}, Lys^{4})(PGL)-6 (■) and poly(Glu^{8}, Lys^{4})-4 (■) antibodies.](https://example.com/fig3)
washed at 4°C with 200 ml of phosphate buffer, then three times with 30 ml of an ice-cold solution of 0.01 N NaOH and finally, with 20 ml of phosphate buffer in order to elute any remaining dissociated R-NT. The three washes with 0.01 N NaOH and the last wash with phosphate buffer were pooled and the solution was rapidly neutralized with 2 N HCl. After the three batches of R-NT-containing solution were processed in that manner on the antibody-Sepharose conjugate, the R-NT remaining in the filtrates and 200 ml washes was recycled after the fractions were examined for R-NT and the two active regions PI and PII were pooled separately and lyophilized (Fig. 4a). PI was rechromatographed on SP-Sephadex in the same conditions as described above (Fig. 4b).

**Preparative Paper Electrophoresis**—The lyophilized material corresponding to PI (about 0.5 mg of protein) was applied to a 10-cm band to Whatman No. 1MM paper and subjected to high voltage electrophoresis at pH 3.0 (Fig. 5). The band was cut into 2-cm strips. The strips were eluted with 0.1 M acetic acid and the eluates were assayed for R-NT.

**RESULTS**

### R-NT Content in Intestinal Tissue

The R-NT content of the initial acetone acid extract of 50 kg of bovine intestinal tissue was 1.7 and 1.5 μmol when measured with poly(Glu6', Lys4')-4 and poly(Glu6', Lys4')-6 antisera, respectively. These results indicate that the concentration of R-NT in intestinal tissue is approximately 35 pmol/g of wet tissue.

**Yields**—Table I summarizes the results of the isolation of R-NT recovered after electrophoresis. A 250,000-fold purification was achieved with an overall yield of approximately 15% for PII. These results are similar to those obtained for

| Purification step | Total protein (mg) | Immunoactivity (nmol) | Yield (%) | Specific activity (nmol/mg) |
|-------------------|--------------------|-----------------------|-----------|--------------------------|
| 80% Acetone extraction | 580,000 | 1,500 | 100 | 0.0026 |
| Adsorption on sulfopropyl Sephadex | 40,000 | 1,200 | 80 | 0.03 |
| First gel chromatography on Sephadex G-25 | 940 | 1,100 | 75 | 1.2 |
| First chromatography on SP-Sephadex | 930 | 670 | 45 | 7.5 |
| Second gel chromatography on Sephadex G-25 | 90 | 250 | 17 | 420 |
| Affinity chromatography | 400 | 27 |
| Second chromatography on SP-sephadex | 0.6 | 250 |
| Paper electrophoresis, pH 3.5 | 0.35* | 200 | 13 | 50 |

* Protein is expressed as absorbance units at 280 nm.

* Protein was calculated from quantitative amino acid analyses.
hypothalamic neurotensin using a somewhat different purification procedure (1).

**Purification**—When chromatographed on Sephadex G-25 (Fig. 1 and Fig. 3) and on SP-Sephadex (Fig. 2), R-NT was recovered in a mean peak co eluting with synthetic neurotensin (indicated by an arrow on the figures). Further purification of R-NT was obtained using affinity chromatography. When 670 nmol of R-NT were chromatographed in several batches (See "Methods") on the immunoabsorbent, 400 nmol of R-NT (as measured by either antisera) were recovered yielding 60% for this purification step. The increase in specific activity, although not measured directly, was estimated to be ca. 50 on the basis of data obtained by chromatography of rat intestinal extracts on the same immunoabsorbent and in the same conditions as described above. When the material post-affinity chromatography was rechromatographed on SP-Sephadex (Fig. 4a) two peaks of R-NT, PI and PII, were obtained. PII (250 nmol) chromatographed in the same regions as synthetic neurotensin while PI (60 nmol) was eluted earlier from the column. Amino acid analysis of PI and PII (Table II) indicated that although other residues were present, both peaks possessed similar molar ratios of the constituent amino acids in neurotensin. In addition, when PI was rechromatographed in the conditions of Fig. 4a, the immunoreactivity was recovered in the same region as synthetic neurotensin and PII (Fig. 4b). These results suggest that PI represents the same material as PII and that it eluted earlier during the initial ion exchange step because of some artifact of the procedure. Finally, when the material contained in PII was submitted to high voltage paper electrophoresis, R-NT was recovered only in a single large peak consisting of four regions A, B, C, and D, with Region C having the same electrophoretic mobility as neurotensin (Fig. 5).

**Composition**—Table III shows the amino acid compositions determined for the material in Regions A, C, and D. Regions A, C, and D had identical compositions to that of neurotensin except for the values of the molar ratio of leucine which were 1.8, 1.4, and 1.1, respectively. Other residues such as glycine, serine, and alanine, present in PII (Table II) were found in very low concentration and are likely to be contaminants. These results suggest that (a) a tridecapeptide having the same amino acid composition as neurotensin is present in Region A; (b) a dodecapeptide having the amino acid composition of neurotensin minus a leucyl residue is present in Region D; and (c) a mixture of these two peptides (about 60% of the dodecapeptide) is found in Region C. The material in Region B was inadvertently dissolved in phosphate buffer which contained gelatin and was not amenable to amino acid analysis.

**Carboxypeptidase Studies of Regions A, C, and D**—The COOH-terminal sequence of neurotensin has been shown to be Tyr-Ile-Leu-OH by kinetic studies involving the treatment of the peptide with carboxypeptidase A (2). The free amino acids released when the materials in Regions A, C, and D were treated with carboxypeptidase A for 3 and 180 min are given in Table IV. Leucine and isoleucine were rapidly released in equal amounts (0.6 residue) from the material in Region A. In contrast, 0.35 and only 0.05 residues of leucine were released from the material in Regions C and D, respectively, even after 180 min, whereas isoleucine was released rapidly from both, 0.7 and 0.6 residues appearing after only 3 min. Tyrosine was released more slowly from the materials in each region, as expected if it is adjacent to a prolyl residue as in neurotensin. These results are consistent with the interpretation stated above (see "Composition"). In addition, they indicate that the COOH-terminal sequence of the tridecapeptide (Region A) is the same as that of neurotensin, whereas the COOH-terminal sequence of the dodecapeptide (Region D) is Tyr-Ile-OH. This sequence of the amino acid compositions of Regions A and D.

**Isolation and Amino Acid Composition of Papain Fragments**

### Table III

| Amino acid | Electrophoresis at pH 3.5 of Peak II | Neurotensin residues |
|------------|-------------------------------------|---------------------|
|            | Region A | Region C | Region D |
| Aspartic acid | 1.1 | 1.0 | 1.0 |
| Glutamic acid | 2.1 | 2.0 | 1.9 |
| Proline | 2.0 | 2.0 | 1.9 |
| Isoleucine | 0.8 | 0.8 | 0.8 |
| Leucine | 1.8 | 1.4 | 1.1 |
| Tyrosine | 1.8 | 1.7 | 1.7 |
| Lysine | 1.0 | 1.0 | 1.0 |
| Arginine | 2.0 | 1.9 | 2.0 |
| Glycine | 0.3 | 0.2 | 0.1 |
| Serine | 0.2 | 0.1 | 0.1 |

### Table IV

| Digestion | Region A | Region C | Region D |
|-----------|----------|----------|----------|
| Leu | Ile | Tyr | Leu | Ile | Tyr | Leu | Ile | Tyr |
| 3 | 0.60 | 0.65 | 0.30 | 0.70 | 0.05 | 0.60 |
| 180 | 0.60 | 0.65 | 0.40 | 0.35 | 0.30 | 0.35 | 0.05 | 0.70 | 0.30 |
of Region C—When neurotensin is digested by the endopeptidase papain, the following are obtained. The NH₂-terminal Fragment P-1 (<Glu-Leu-Tyr-Glu-OH), the middle Fragment P-2 (Asn-Lys-Pro-Arg-OH), and the COOH-terminal Fragment P-3 (Arg-Pro-Tyr-Ile-Leu-OH) (2). Such a digestion was performed on neurotensin and R-NT from Region C (because it contained the most material) and the electrophoretic mobilities of the resulting fragments were compared (Fig. 6). Region C yielded four fragments; three of them, P'-1, P'-2, and P'-3 show the same electrophoretic mobilities as P-1, P-2, and P-3, respectively. P'-4 has a mobility slightly higher than that of P-3. The amino acid compositions determined for these fragments are shown on Table V and are compared to the theoretical compositions of the corresponding fragments obtained from neurotensin. Near integral molar ratios of the constituent amino acids were obtained for each of the fragments; the compositions of P'-1, P'-2, and P'-3 were similar to those of P-1, P-2 and P-3, respectively. The additional Fragment P'-4 was found to have the composition of P-3 minus a leucyl residue; this might account for its slightly higher electrophoretic mobility (Fig. 6). Approximately 3 times as much P'-4 was obtained as P'-3, which is consistent with the interpretation that the R-NT used to generate those fragments (Region C, Fig. 5) consisted of about 40% tridecapeptide and 60% dodecapeptide, and upon treatment with papain these peptides yielded the COOH-terminal fragments, P'-3 and P'-4, respectively.

**Biological Activity**—The effects of neurotensin, Region A (tridecapeptide), and Region D (dodecapeptide) on the systemic blood pressure of anesthetized rats are compared in Fig. 7. Synthetic neurotensin and Region A at 500 pmol/kg are comparable in inducing hypotension in the rat. In contrast, Region D at a dose about 3 times higher than that of neurotensin and Region A, shows no effect on the systemic blood pressure of the anesthetized rat.

**DISCUSSION**

A tridecapeptide (Region A) with the same amino acid composition as that of neurotensin has been isolated from extracts of bovine intestinal tissues. This peptide has immunological, chromatographic, and electrophoretic properties indistinguishable from those of neurotensin. Carboxypeptidase treatment of the isolated peptide indicated that the COOH-terminal sequence was the same as that of neurotensin. In addition, this material was as potent as neurotensin in inducing hypotension in anesthetized rats. This strongly suggests that the intestinal tridecapeptide is identical to hypothalamic neurotensin and it will be referred to as intestinal neurotensin. Another peptide which is likely to be the neurotensin (1-12) dodecapeptide (Region D) has also been isolated and separated from the tridecapeptide by high voltage paper electrophoresis. The finding that this dodecapeptide had no detectable effect on the systemic blood pressure of anesthetized rats confirms the requirement of the COOH-terminal region of neurotensin for its biological activity (7). It is reasonable to assume that this dodecapeptide has been generated from intestinal neurotensin prior to the extraction procedure. The degradation of intestinal neurotensin by carboxypeptidases might possibly be the mechanism by which the intestinal neurotensin is biologically inactivated in vivo. The heterogeneity of R-NT was not indicated by the radioimmunoassays performed during the purification procedure. When the materials isolated in Regions A and D were carefully assayed with both poly(Glu⁶⁶, Lys⁴⁷)-4 and poly(Glu⁶⁶, Lys⁴⁷)-6 antisera, it was found that the tridecapeptide (Region A) had the same immunological activity as neurotensin, whereas the

![Fig. 6. Drawing of the patterns of stainable material obtained after high voltage paper electrophoresis of papain digests of neurotensin and Region C. R-NT (40 nmol) from Region C was digested with papain during 4 h at 38°C in 0.03 M ammonium acetate (pH 5.5), 0.03 M mercaptoethanol with an enzyme to substrate molar ratio of 1:50. Of this material, 35 nmol were applied across 6 cm at the origin. The amount of the different peptides eluted from the paper is indicated in nmol. Other materials were spotted as follows. S, standards; P, papain digest of neurotensin (5 nmol); P', papain digest of Region C (5 nmol). Conditions: pH 8.5, 50 min at 86 V/cm; peptides and standards were stained with the chlorine, o-toluidine method.]( attachment: image.png)

**Table V**

| Amino acid | Fragments |
|------------|-----------|
|            | P-1 | P-2 | P-2 | P-3 | P-3 | P-4 |
| Aspartic acid | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 |
| Glutamic acid  | 2.0 | 2.0 | 1.1 | 1.1 | 1.1 | 1.1 |
| Proline       | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Isoleucine    | 0.9 | 0.9 | 0.9 | 0.9 | 0.9 | 0.9 |
| Leucine       | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Tyrosine      | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Lysine        | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Arginine      | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Total residues| 44  | 44  | 44  | 44  | 44  | 44  |
| Yield %       | 98  | 98  | 98  | 98  | 98  | 98  |

*Calculated as mol of peptide Pi/mol of R-NT from Region C determined by amino acid analysis.
interesting to notice that the vasoactive intestinal polypeptide, although structurally different from neurotensin (3, 9) exhibits several pharmacological properties similar to those of neurotensin, i.e. both induce systemic vasodilation, hypotension, hyperglycemia, and contraction of ileal smooth muscle (10-12).

Another possibility is suggested from what is known about the sialogogic peptide, Substance P. Substance P has been isolated and characterized from both hypothalamic (13) and intestinal tissues (14), a situation which resembles that of neurotensin and intestinal neurotensin. Studies on the localization of Substance P in the gastrointestinal tract indicate that the peptide is mainly localized to the nerve plexuses innervating the gastrointestinal tract (15). In addition, Substance P may participate in chemical neurotransmission (16). Similar studies should be valuable in elucidating the role of both neurotensin and intestinal neurotensin.

**Acknowledgments**—We are grateful for the excellent technical assistance afforded by Miss Elise Camelio and Mr. John Dryer. We wish to thank Dr. Clyde Zalut and Mr. Michael Spellman who performed the quantitative amino acid analysis.

**REFERENCES**

1. Carraway, R., and Leeman, S. E. (1973) *J. Biol. Chem.* 248, 6854-6861
2. Carraway, R., and Leeman, S. E. (1975) *J. Biol. Chem.* 250, 1907-1911
3. Carraway, R., and Leeman, S. E. (1975) *J. Biol. Chem.* 250, 1912-1918
4. Carraway, R., and Leeman, S. E. (1974) *Fed. Proc.* 33, 458
5. Carraway, R., and Leeman, S. E. (1976) *J. Biol. Chem.* 251, 7035-7044
6. Carraway, R., and Leeman, S. E. (1976) *J. Biol. Chem.* 251, 7045-7052
7. Carraway, R., and Leeman, S. (1975) in *Peptides: Chemistry, Structure and Biology* (Walter, R., and Meinhofer, J., eds) p. 679, Ann Arbor Science, Ann Arbor
8. Grossman, M. I., (1974) *Gastroenterology* 67, 730-755
9. Bodanszky, M., Klausner, Y. S., and Said, S. I. (1973) *Proc. Natl. Acad. U. S. A.* 70, 382-384
10. Said, S. I., and Mutt, V. (1970) *Science* 169, 1217-1218
11. Said, S. I., and Mutt, V. (1972) *Eur. J. Biochem.* 28, 199-204
12. Piper, P. J., Said, S. I., and Vane, J. R. (1970) *Nature* 225, 1144-1146
13. Chang, M. M., and Leeman, S. E. (1970) *J. Biol. Chem.* 245, 4784-4790
14. Studer, R. O., Trzeciak, H., and Lergier, W. (1973) *Helv. Chim. Acta* 56, 890-866
15. Pearse, A. G. E., and Polak, J. M. (1975) *Histochemistry* 41, 373-375
16. Otsuka, M., Konishi, S., and Takahashi, T. (1972) *Proc. Jap. Acad.* 48, 747

---

**Intestinal Neurotensin**

![Figure 7. Effects of synthetic neurotensin, Regions A, and D on the systemic blood pressure of anesthetized rats.](image-url)
Isolation of a tridecapeptide from bovine intestinal tissue and its partial characterization as neurotensin.

P Kitabgi, R Carraway and S E Leeman

*J. Biol. Chem.* 1976, 251:7053-7058.

Access the most updated version of this article at [http://www.jbc.org/content/251/22/7053](http://www.jbc.org/content/251/22/7053)

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 0 references, 0 of which can be accessed free at [http://www.jbc.org/content/251/22/7053.full.html#ref-list-1](http://www.jbc.org/content/251/22/7053.full.html#ref-list-1)