

basis of foregoing discussion the compounds may be assigned a polymeric octahedral structure containing bridging (bidentate) oxalate groups as shown in Fig. 1.

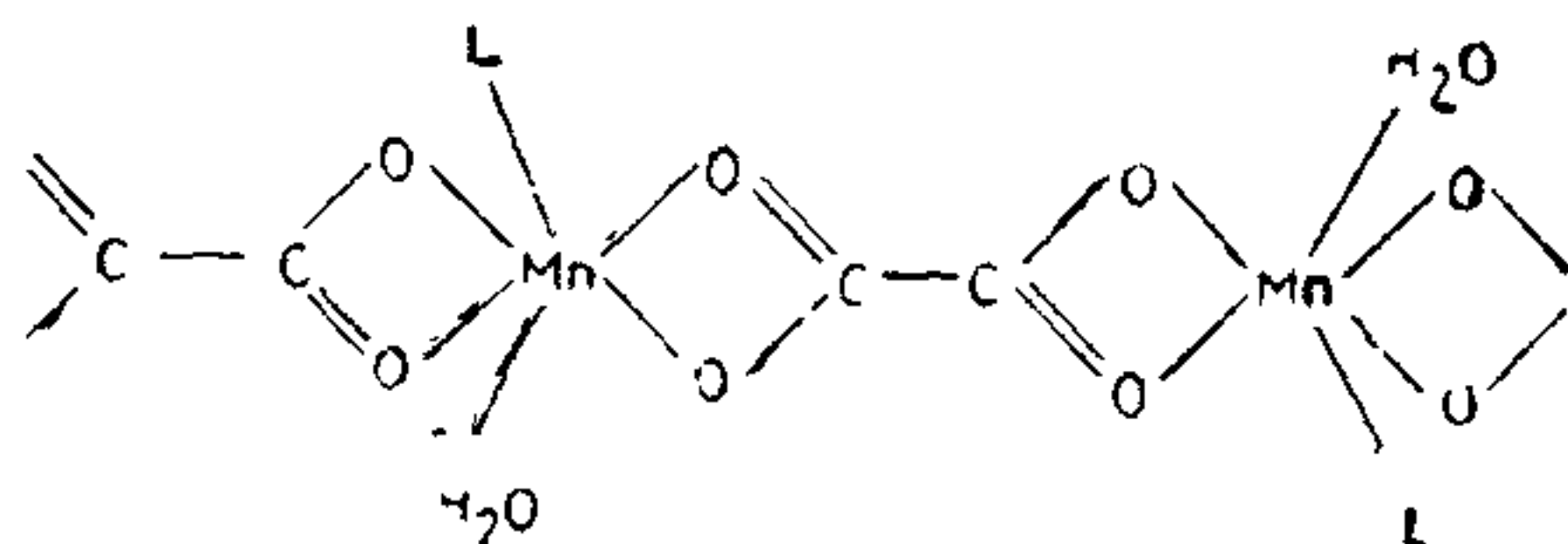


FIG. 1. Structure of $MnC_2O_4 \cdot L \cdot H_2O$

TABLE V

Electronic spectral data for some Mn(II) complexes

Compound	λ_{max} (cm ⁻¹)
$MnC_2O_4 \cdot U \cdot H_2O$	27000, 22730, 16210
$MnC_2O_4 \cdot TU \cdot H_2O$	26800, 22500, 16110
$MnC_2O_4 \cdot DMF \cdot H_2O$	27000, 23100, 16380
$MnC_2O_4 \cdot Pf \cdot H_2O$	27100, 22640, 16220
$MnC_2O_4 \cdot Quin \cdot H_2O$	26800, 21850, 16190

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- Liptay, G. and Burger, K., *J. Inorg. Nucl. Chem.*, 1969, 31, 2359.
- Das, A. K. and Ramana Rao, D. V., *J. Ind. Chem. Soc.*, 1971, 48, 823.
- Forster, D. and Goodgame, D. M. L., *J. Chem. Soc.*, 1964, p. 2790.

- Wheeler, S. H., Zingheim, S. C. and Nathan, L. C., *J. Inorg. Nucl. Chem.* 1978, 40, 778.
- Arena, G., Bonomo, R. P., Rizzarelli, E. and Seminara, A., *Inorg. Chim. Acta*, 1978, 30, 13.
- Gurrien, S., Musumeci, S., Rizzarelli, E. and Seminara, A., *J. Inorg. Nucl. Chem.*, 1976, 38, 1215.
- Shkodina, T. B., Zhdanovskikh, T. M. and Nikonenko, E. A., *Chem. Abstr.*, 1975, 83, 201384r.
- Vogel, A. I., *Quantitative Inorganic Analysis*, Third edition, ELBS, Longmans, Green and Co. Ltd., London, 1961.
- Penland, R. B., Mizushima, S., Curran, C. and Quagliano, J. V. *J. Am. Chem. Soc.*, 1957, 79, 1575.
- Stancheva, Peya, *Chem. Abstr.*, 1971, 74, 60364j.
- Swaminathan, K. and Irving, H. M. N. H., *J. Inorg. Nucl. Chem.*, 1964, 26, 1291.
- Archambault, J. and Rivest, R., *Canad. J. Chem.*, 1960, 38, 1331.
- Cotton, F. A., Francis, R. and Horrocks, W. D., *J. Phys. Chem.*, 1960, 64, 1534.
- Paul, R. C. and Chadha, S. L., *Indian J. Chem.* 1968, 6, 272.
- Clark, R. J. H. and Williams, C. S., *Inorg. Chem.*, 1965, 4, 350.
- Ahuja, I. S., *J. Inorg. Nucl. Chem.*, 1967, 29, 2091.
- Jeffery, G. A. and Parry, G. S., *J. Am. Chem. Soc.*, 1954, 76, 5283.
- Nakamoto, K., *Infrared Spectra of Inorganic and Coordination Compounds*, Wiley-Interscience, John Wiley and Sons, Inc., New York, 1970.
- Porajkoshts, M. A. and Tishchenko, G. N., *Kristallografiya*, 1959, 4, 239.
- Zaborenko, K. B., Kung, S., Molikhov, L. L. and Portyanovi, V. A., *Chem. Abstr.*, 1965, 62, 11394a.

NEW INDOLYL HYPOTENSIVE AGENTS

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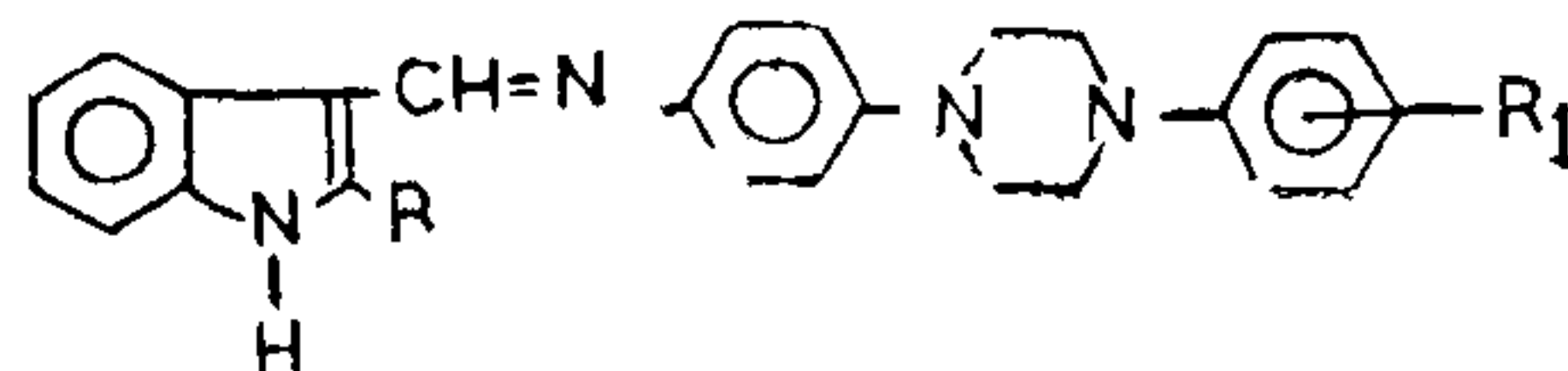
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SOME new 2-substituted-3-[[p-(N⁴-aryl-N¹-piperaziny) anilino] methyl] indoles have been prepared by the condensation of 2-substituted indole-3-aldehyde with 1,4-disubstituted piperazines followed by the reduction of the imine linkage by palladium carbon in N,N-dimethyl formamide and hydrazine hydrate to give the title compound. All the compounds were screened for their cardiovascular activity. Some of the compounds possess cardiovascular activity.

The presence of an indole nucleus in both naturally occurring and synthetic antihypertensive compounds¹⁻⁴ and the important role of 5-HT in the cardiovascular disorders have initiated a great spurt in the investigation of a number of analogues for cardiovascular activity⁵⁻⁸. In addition, the clinical efficiency of numerous indole derivatives⁹⁻¹¹ for the treatment of cardiovascular disorders and their ability to lower the blood pressure have prompted the synthesis of 2-substituted-3-[[p-(N⁴-aryl-N¹-piperaziny) anilino] methyl] indoles and evaluated them for their cardiovascular activity.

* For correspondence.

TABLE I

2-Substituted-3-[[p-(N⁴-aryl-N¹-piperazinyl)] phenyl-aldimino] indole

Sl. No.	R	R ₁	M.P. °C (a)	Yield %	Molecular formula	% change in blood pressure*	ALD ₅₀ mg/kg (I.P.)
1.	H	H	175	60	C ₂₅ H ₂₄ N ₄	-29.2	1000
2.	H	2-CH ₃	198	55	C ₂₆ H ₂₆ N ₄	-43.1	1000
3.	H	4-CH ₃	205	55	C ₂₆ H ₂₆ N ₄	-12.6	1000
4.	H	2-Cl	194	60	C ₂₅ H ₂₃ N ₄ Cl	-10.1	500
5.	CH ₃	H	204	55	C ₂₆ H ₂₆ N ₄	-29.8	500
6.	CH ₃	2-CH ₃	220	50	C ₂₇ H ₂₈ N ₄	-31.0	1000
7.	CH ₃	4-CH ₃	188	55	C ₂₇ H ₂₈ N ₄	-65.1	500
8.	CH ₃	2-Cl	198	65	C ₂₆ H ₂₅ N ₄ Cl	-11.2	500
9.	C ₆ H ₅	H	180	50	C ₃₁ H ₂₈ N ₄	-60.9	500
10.	C ₆ H ₅	2-CH ₃	215	55	C ₃₂ H ₃₀ N ₄	-54.1	1000
11.	C ₆ H ₅	4-CH ₃	235	55	C ₃₂ H ₃₀ N ₄	-43.2	1000
12.	p-CH ₃ · C ₆ H ₄	H	220	50	C ₃₃ H ₃₀ N ₄	-75.6	500

(a) Melting points were taken in open capillary tubes and are uncorrected.

(b) All the compounds were administered (i.v.) in a dose of 2 mg/kg.

(c) The % nitrogen in the compounds agreed with the calculated values.

* Indicates % decrease in blood pressure.

EXPERIMENTAL

Substituted indoles and 2-(alkyl or aryl)-4-indole-3-aldehyde

2-Methyl indole¹², 2-phenylindole¹³, 2-(4-methylphenyl) indole¹⁴ and 2-(alkyl or aryl) indole-3-aldehyde¹⁵ were prepared by the methods reported in literature.

1,4-Disubstituted piperazines

1-(p-nitrophenyl)-4-(p-substituted phenyl) piperazines and 1-(p-aminophenyl)-4-(p-substituted phenyl) piperazines¹⁶ were prepared by the method reported in literature.

2-Substituted-3-[[p-(N⁴-aryl-N¹-piperazinyl) phenyl]-aldimino] indole

A mixture of 2-(alkyl or aryl) indole-3-aldehyde (0.01 mole), 1-(p-aminophenyl)-4-(p-substituted phenyl)-piperazine (0.01 mole) in ethanol (50 ml, dry) was refluxed for six hours. A solid obtained on cooling was filtered and recrystallized from a mixture of ethanol/

petroleum ether. The melting points, yields and other analytical data of the compounds are given in Table I.

2-Substituted-3-[[p-(N⁴-aryl-N¹-piperazinyl) anilino] methyl] indole

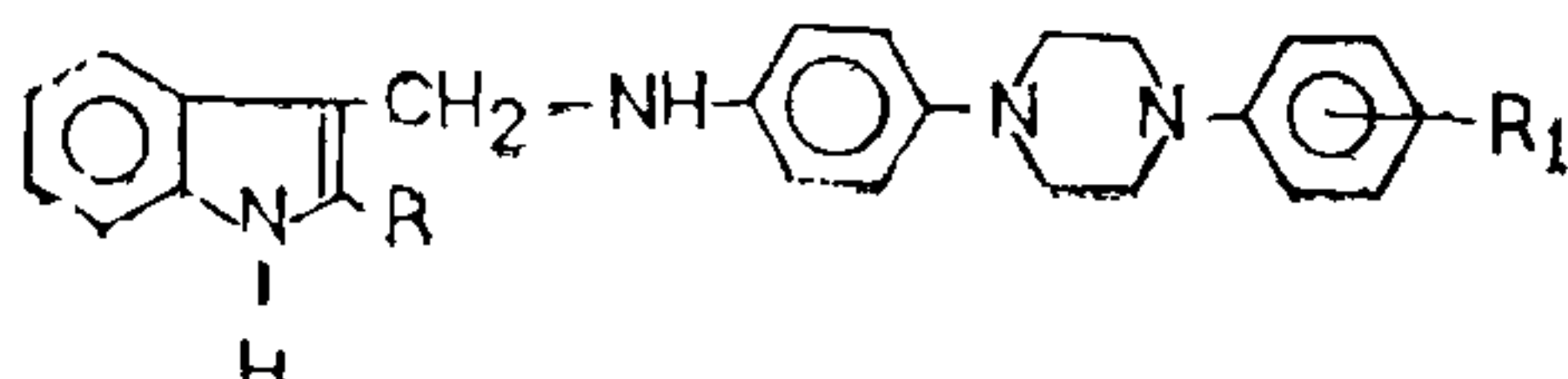
A mixture of 2-substituted-3-[[p-(N⁴-aryl-N¹-piperazinyl)-phenyl] aldimino] indole (0.005 mole) and hydrazine hydrate (98%, 0.02 mole), was refluxed in N,N-dimethylformamide (50 ml) with a small amount of palladium carbon (10%, 0.3 gm) for 10 hours. The reaction mixture was filtered hot and was poured into ice cold water, extracted with ether and dried over anhydrous sodium sulfate, concentrated in vacuo to yield a solid which was recrystallized from a mixture of ethanol/ether. The melting points, yields and other analytical data of the compounds are reported in Table II.

Pharmacological Studies

The present investigation was carried out on adult mongrel dogs of either sex weighing between 12-20 kg. The dogs were anaesthetized with pentobarbitone

TABLE II

2-Substituted-3-[[p-(N⁴-ary-N¹-piperaziny) anilino] methyl] indole



Sl. No.	R	R ₁	M.P. °C (a)	Yield %	Molecular formula	% change in blood pressure*	ALD ₅₀ mg/kg (I.P.) (c)
13.	H	H	128	50	C ₂₅ H ₂₆ N ₄	-22.2	1000
14.	H	2-CH ₃	168	40	C ₂₆ H ₂₈ N ₄	±0	..
15.	H	4-CH ₃	136	45	C ₂₆ H ₂₈ N ₄	±0	—
16.	H	2-Cl	155	40	C ₂₅ H ₂₅ N ₄ Cl	±0	—
17.	CH ₃	H	146	45	C ₂₆ H ₂₈ N ₄	-43.7	1000
18.	CH ₃	2-CH ₃	138	45	C ₂₇ H ₃₀ N ₄	±0	—
19.	CH ₃	4-CH ₃	120	50	C ₂₇ H ₃₀ N ₄	±0	—
20.	CH ₃	2-Cl	132	40	C ₂₆ H ₂₇ N ₄ Cl	±0	—
21.	C ₆ H ₅	H	112	45	C ₃₁ H ₃₀ N ₄	-48.0	1000
22.	C ₆ H ₅	2-CH ₃	126	45	C ₃₂ H ₃₂ N ₄	±0	—
23.	C ₆ H ₅	4-CH ₃	130	40	C ₃₂ H ₃₂ N ₄	±0	—
24.	p-CH ₃ . C ₆ H ₄	H	122	50	C ₃₂ H ₃₂ N ₄	-12.5	1000

(a) Melting points were taken in open capillary tube and are uncorrected.

(b) All the compounds were administered in a dose of 2 mg/kg (I.V.).

(c) — indicates that the drug was not tested.

(d) The % nitrogen in the compounds agreed with the calculated values.

sodium (30 mg/kg i.v.). The blood pressure was recorded from the left common carotid artery by means of mercury manometer on smoked kymograph paper. The carotid occlusion and noradrenaline responses were evoked by either occluding both the carotid arteries (carotid occlusion response) or by injecting 1-2 µg/kg of noradrenaline intravenously. The effect of newly synthesized compounds was studied on resting blood pressure and on the responses evoked by bilateral carotid occlusion (CO) and noradrenaline (NA) injection.

The cardiovascular effects of newly synthesized compounds are given in Tables I and II.

Acute Toxicity Study

The approximate 50% lethal dose (AID₅₀) of the active compounds under study was determined in albino mice of either sex according to the reported method¹⁷,

RESULTS AND DISCUSSION

Among the twenty-four compounds tested sixteen compounds (1-13, 17, 21 and 24) induced transient fall in systemic blood pressure ranging from -20 to -120 mm of Hg without effecting the carotid occlusion and noradrenaline responses.

Maximum hypotensive activity was observed in two compounds (7 and 12) which lasted for about 30 minutes. The remaining eight compounds (14, 15, 16, 18, 19, 20, 22 and 23) failed to exhibit any cardiovascular effect.

The study shows that the reduction of the imine linkage resulted either in complete loss of activity (14, 15, 16, 18, 19, 20, 22 and 23) or in decrease in the activity (13, 21 and 24) except in case of compound 17, which was more active than the parent compound (5). None of these compounds could effect the carotid occlusion response and noradrenaline response,

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- Schlittler, E. and Bein, H. J., In *Antihypertensive Agents*, E. Schlittler, ed., Academic Press, New York, 1967, p. 191.
- Erspamer, V. and Asero, B., *Nature (London)*, 1952, 169, 800.
- Shaw, E. and Wooley, Q. W., *J. Pharmacol. Exptl. Therap.*, 1954, 111, 439.
- Arnold, A., Selberies, W. H., *Experientia*, 1967, 23, 298.
- Hukner, Charles, F., *Ger. Offen*, 2, 609, 289 (Cl. 007 2401/14) 30 Sept. (1976)- *U.S. Appl.* 556, 600, 10 March, 1975, 72 pp.
- Archibald, John, L., Takson, John Lambert, *Brit.*, 1, 413, 708 (Cl. 007D, 461K) Nov. (1975), *Appl.*, 29, 156/73, 19 June (1973), 2 pp, Add. to *Brit.*, 1, 218, 570.
- Alps, B. J., Archibald, J. L., Johnson, E. S. and Wilson, A. B., *Cardiovasc. Res.*, 1970, p. 62.
- Alps, B. J., Tull, N., Johnson, E. S. and Wilson, A. B., *Ibid.*, 1970, 40, 153.
- Rapport, M. M., Green, A. A., Page, J. H., *Science*, 1948, 108, 329.
- Rapport, M. M., *J. Biol. Chem.*, 1949, 180, 961.
- Hamlin, K. E. and Fisher, F. E., *J. Am. Chem. Soc.*, 1951, 73, 5007.
- Allen, C. F. H. and VauAllan, *J. Org. Syn. Coll.*, 1955, 3, 597.
- Vogel, I., *A Textbook of Practical Organic Chemistry*, 1971, 851, 852.
- Albro, L. P., Baltzly, R. and Phillips, A. P., *J. Org. Chem.*, 1949, 74, 771.
- Jerry, A., Weisbach, Edward, Macko, Nicholas, J. De, Sanctis Michael, P., Cacava and Bryce Douglas, *J. Med. Chem.*, 1964, 7, 738.
- Dubey, M., Verma, V. K., Shanker, K., Sinha, U. N., Bhargava, K. P. and Kishor, K., *Pharmazie*, 1978, 33 (10), 640.
- Smith, C. C., *J. Pharmacol. Exp. Ther.*, 1943, 77, 392.

ESTIMATION OF RARE EARTH COMPLEXES OF GLUTAMIC ACID WITH CHLORAMINE-T AND CHLORAMINE-B

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ABSTRACT

Chloramine-T (CAT) and Chloramine-B (CAB) have received considerable attention as oxidimetric reagents¹⁻⁴. The mono sodium salt of glutamic acid finds extensive commercial use as a flavour intensifier, while the acid itself is used in medicine and biochemical research, and as a salt substitute and dietary supplement. Rapid methods have been developed for the estimation of this amino acid^{5,6} in solution with CAT and CAB. In view of the importance of the metal protein complexes in organic chemistry, a study of metal-amino acid complexes is worthwhile as these are helpful in the separation and identification of amino acids. The present communication reports an elegant method for the estimation of trivalent rare earth complexes of glutamic acid with CAT and CAB.

MATERIALS AND METHODS

THE rare earth complexes of glutamic acid having the general formula $M(\text{glut-H})_3 \cdot 3\text{H}_2\text{O}$ where M is Y, La, Pr, Nd, Sm, Gd, Tb, Dy and Ho were prepared by mixing stoichiometric amounts of amino acid and the rare earth carbonate in aqueous solution⁷. The composition was checked by determining the rare earth content by the oxalate method⁸. Chloramine-T

was purified by the method of Morris *et al.*⁹. Chloramine-B was prepared¹⁰ by passing chlorine through benzene sulphonamide dissolved in 4N NaOH solution over a period of one hour at 70°. The mass obtained was filtered, dried and crystallised from water. Approximately decinormal aqueous solutions of CAT and CAB were prepared and standardised by the iodometric method.