

Preparation of Cobalt Complex Compound of Chlorophyllin

By

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崔宗仁 : Chlorophyllin cobalt Complex 化合物의 製造에 關한 研究

Magnesium Chlorophyllin 으로부터 常法에 依하여 製造한 Chlorin-e 에 水溶性 Cobalt 鹽을 作用시켜 Chlorophyllin 에 Cobalt Complex 化合物을 製造하였다. Chlorin 製法에 있어서 alcohol 溶媒를 使用해 온 方法은 Chlorin 이 alcohol 에 對한 溶解度가 極히 적은 關係로 目的物을 良好한 收待率로 얻지 못할 뿐만 아니라 이에 따르는 操作도 복잡 불편하였으나 溶媒를 水醋酸으로 代置하므로써 좋은 成果를 얻을 수가 있었다.

It has been well known that chlorophyll derivative has a particular action pharmacologically especially for granulation tumor.

Various metallic derivatives of chlorophyll has been used in proprietary products for removing objectionable odors,¹⁾ According to Moss *et al*²⁾ an ointment containing water soluble chlorophyll has excellent deodorant power for suppurating wounds and ulcers.

The Compounds has also been recommended for control of body and breath odors,^{3,4)} a usage which may provide a large market for chlorophyll derivatives.

Within the last few years interest in cobaltous chlorophyllin has marketly increased. It has been known that the chlorophyllin derivatives which has cobalt in the center of chlorophyllin molecule instead of magnesium has worth action pharmaceutically.⁵⁾

L.S. Hiraoka⁶⁾ reported that cobalt chlorophyllin derivative was obtained from silkworm feces which is the by-product in the silk industry, but the method can not be considered as the practical method, since the yield is too low (0.02%—0.025% of the starting material, 2% of chlorophyllin), and the procedure is complicated. Therefore it can be thought that no method of preparing cobaltous chlorophyllin which can be used practically is reported in detail, although several attempts have been made,^{7,8)} for the purpose of preparation of metallic especially, cobalt chlorophyllin derivatives.

In this experiment relatively good result in preparation of cobaltous chlorophyllin was obtained. Author believes that the compound obtained in this experiment can be used as a starting material of other cobalt chlorophyllin derivatives and it is enough to use this cobalt chlorophyllin externally for the therapeutical purpose, although the compound obtained does not have so high purity. (70—80%)

The process to be described involves the preparation of cobaltous chlorophyllin from water soluble magnesium chlorophyllin which can be obtained cheaply.

The three following reactions are involved in the conversion of water soluble magnesium chlorophyllin which is produced by well known process from plants.

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slowly added stirring vigorously. The mixture was heated at 80° for one hour. After cool, the precipitated cobalt chlorophyllin was filtered and washed thoroughly with hot, slightly acidified water, and dried by suction. On the purpose of purifying cobalt chlorophyllin thus obtained, the impure compound was suspended in ethanol (10 ml—20 mls. per one gram of derivative, moisture free basis).

It was refluxed for one half hour with an equal volume of ethanol containing the theoretical quantity of sodium hydroxide required for reaction with the cobalt chlorophyllin. For every gram of 100 per cent cobalt chlorophyllin, moisture free basis, 0.183 gram of sodium hydroxide is required. Since excess alkali may decompose the cobalt complex compound, the purity of the cobalt chlorophyllin should be carefully determined and appropriate adjustments of the quantity of alkali made if necessary. For example, if the cobalt derivative is 50 per cent pure, then $0.183 \times 0.50 = 0.0915$ grams sodium hydroxide would be required for every gram of derivative. The resultant solution was filtered, any insoluble material was washed with 50 percent aqueous ethanol, and the filtrate was neutralized by hydrochloric acid to pH 7.2 and filtered.

The filtrate was slightly acidified by hydrochloric acid (pH 4.0—4.5). Then relatively purer cobalt chlorophyllin was precipitated.

The precipitate was washed with water, alcohol and ether and dried.

Although alcohol was often used as a solvent in preparation of metallic chlorophyllin compound, glacial acetic acid was used as the solvent in this experiment. The advantage of this method is as follows:

1. smaller amount of solvent is needed in comparison with other method.
2. the yield is very high.
3. the procedure is relatively simple.

Preparation of Sodium Cobalt Chlorophyllin.—The solution obtained by the same process as the purification process was concentrated to dryness on a steambath.

The yields based on cobalt chlorophyllin are almost quantitative. The purity of the product based on cobalt analysis ranges from 70% to 80%.

Determination of Cobalt.—The cobalt content is one of the criteria of the purity of cobaltous chlorophyllin and sodium cobaltous chlorophyllin.

Theoretically, the former compound contains 9.035 per cent cobalt and the latter 8.17 per cent.

A sample of approximately 0.1 gram (moisture-free basis) is digested with 3 mls—10 mls of concentrated sulfuric acid in Kjeldahl tube. When all frothing and foaming ceases and the color of the solution turns black to brown or light brown (this process takes 2 to 4 hours), the solution is cooled. Ten to fifteen drops of 35% perchloric acid is added, and the solution is boiled until it turns colorless or light red (10 to 20 minutes). This solution is cooled, and diluted to 50 mls, and an aliquot is taken for analysis. A colorimetric method involving formation of a blue cobaltous thiocyanate ion was used.⁹⁾

Since the chlorine and cobalt chlorophyllin preparations can not be heat dried, they will have variable water and organic solvent content. The conversion of chlorine to cobaltous chlorophyllin and sodium cobalt chlorophyllin is based on weights calculated to a moisture-free basis. Hence every new batch of these compounds must have an analytical moisture determination. This is simply done

by weighing accurately 1.0 to 2.0 grams of chlorophyllin derivatives and drying to constant weight in vacuum oven at 60°—70°C.

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REFERENCES

1. Westcott. H.F., *N.Y. State J. Med.*, **50**, 698(1950)
2. Paschal G.S., *U.S. Patent*, **2**, 326, 672(1943)
3. Moo *et al.*, *Biochem. Z.*, **324**, 536(1953)
4. Serhing, M.E. *Vet. Med.*, **45**, 291(1950)
5. A.D. Powell, *J. Soc. Chem. Chem. Ind.*, **36**, 273(1917)
E.S. Tomula, *Z. Anal. Chem.*, **83**, 6(1931)
H.M. Putsche, *Anal. Chem.*, **19**, 236(1947)
6. Westcott. H.F., *N.Y. State J. Med.*, **50**, 648(1950)
Moo *et al.*, *Biochem. Z.*, **323**, 439(1953)
7. Hiraoka, J. P., 4945. 28.
- 8.—9. Stomura *J.P.*, **33** 945 Feb. 15(1958); *J.P.* 32, 5729.
Etdr. *Ber. Nat. Konrad L. Zirm.*
Lannach (Steiermark) *osterreichisches Patentant*, 178162.
10. Monroe E. Wall, *U.S.D.A.*, 1951(March), AIC 299.