

The Possible Discovery of a Reagent for Cancer Diagnosis by Urine NMR Analysis*

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= Abstract =

From the analysis of proton NMR signals of human urine it is found that the signals corresponding to a phenolic compound of tyrosine are more frequently observed in cancer urine than in non-cancer urine.

An effective reagent is obtained to detect the substance excreted in the urine and to find out a close connection with the result of the NMR analysis. An attempt is made to determine the reagent sensitivity and specificity for cancer diagnosis. The results of the attempt are respectively above 75% for both on an average.

1. INTRODUCTION

It is well known that tyrosine and other amino acids are excreted in human urine¹⁾, yet the results²⁾ obtained from NMR measurement of the urine by an 80 MHz FT proton NMR spectrometer show that four proton NMR signals between 7.00 ppm and 8.00 ppm which are not observed by a 60 MHz proton NMR spectrometer^{3~5)} are distinctively obse-

erved in the urine.

Moreover from the results²⁾ obtained from many repeated NMR experiments on the urine it is found that the signals which are supposed to correspond to one of the phenolic compounds of tyrosine and its complexes⁶⁾ are more frequently observed in cancer urine than in normal and other diseased urine which are, from now on, called the non-cancer urine for convenience.

On the assumption that the signals are caused by one of the substances excreted in the urine an effective green colored reagent** is obtained from the mixture of mercury, nickel, nitric acid and distilled water to observe the urine reaction precipitates with magenta caused by the excretion.

Like the result of the NMR analysis mentioned above it is found that the precipitates

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**The patent application number given by the Korea Patent Bureau is No. 2511.

***The patent number of the reagent approved by the Korea Patent Bureau is No. 21558. The reagent has the same effect as the green one.

are more frequently observed in the cancer urine than in the non-cancer urine.

In this study an attempt is made to determine the reagent sensitivity and specificity for a differential diagnosis between the cancer and non-cancer urine. The results of the attempt are respectively above 75% for both on an average.

2. Reagent and its sensitivity and specificity

The following processes are taken to obtain the reagent: 1) 5 grams of nickel are dissolved in 50 milliliters of nitric acid. 2) 50 grams of mercury are dissolved in 50 milliliters of nitric acid. 3) The mixing ratio of the solution made by the first process, the solution made the second process and distilled water for the reagent is 2 : 1 : 3.

The followings are taken for the diagnosis by the reagent and for the determination of the sensitivity and specificity: 1) 0.15 milliliter of the reagent is added to 3 milliliters of urine in a test tube to observe the reaction precipitates. 2) The precipitates with magenta are diagnosed as cancer (or as the cancer urine). 3) The precipitates with other colors are diagnosed as non-cancer (or as the non-cancer urine). 4) The sensitivity and specificity are respectively given by

$$\text{Sensitivity} = \frac{N_p}{N_t - N_c}$$

$$\text{Specificity} = \frac{N_n}{N_t - N_c}$$

where N_t is the total number of persons with the cancer and non-cancer urine, N the number of persons with the non-cancer urine, N_c the number of persons with the cancer urine, N_p the number of positive reactions which indicate the precipitates with magenta and N_n the number of negative reactions which indicate the precipitates with other colors.

3. RESULTS AND DISCUSSION

The green reagent made by the mixing ratio indicated in the preceding section very sensitively reacts to urine. This is due to the fact that the mixture, nickel, acts as a good catalyst for an organic synthesis.

Furthermore from many repeated urine reaction tests with different amounts of the reagent it is found that 0.15 milliliter of the reagent for 3 milliliters of urine is the most appropriate amount for obtaining the stable and abundant reaction precipitates.

Another colorless and transparent reagent similar to the green reagent can be obtained by the two mixtures such as mercury dissolve in nitric acid and distilled water excluding nickel. Such a reagent is known as one of the Millon reagents.

However the reagent made by the mixtures is not so effective in comparison with the green one; when the reaction precipitates in the test tube formed by the colorless reagent are agitated for a while the precipitates almost disappear or the precipitates are considerably decreased.

As indicated in the introductory remarks the precipitates with magenta are occasionally observed even in the non-cancer urine, however it is easily observed that the excretion concentration in the urine is relatively so lower than in the cancer urine that only the characteristic color of the precipitates mostly disappears by giving an agitation just as mentioned above.

In this case the urine is diagnosed as non-cancer. On the contrary such does not occur in the cancer urine. However it must here be mentioned that the precipitates with the color are not occasionally observed even in the cancer urine.

Sometimes it is a little difficult to make the differential diagnosis because the same reaction precipitates with the characteristic color are obtained from both the cancer and non-cancer urine.

But very careful observation made by human eyes indicates that the precipitate color of the cancer urine caused by the reagent is slightly deeper than the one of the non-cancer urine. If one uses an appropriate spectrometer, the color of the cancer urine can clearly be distinguished from the one of the non-cancer urine. In this way, it is obvious that a better sensitivity and specificity of the reagent can be obtained.

It does not seem to have need to show all the results diagnosed by the reagent and authorized university hospitals to ascertain the average value of the sensitivity and specificity indicated in the introductory remarks, but it is worthwhile to introduce the results of references 3 and 2 which are obtained by the reagent*** made by mercury dissolved in nitric acid, distilled water and gelatine ; the results of reference 3 are respectively 79.2 % for sensitivity and 75.0% for specificity

and the results of reference 2 are respectively 85.3% for sensitivity and 91.4% for specificity.

In conclusion, although neither the exact identification of the excretion nor the classification of kinds of cancer can be made by the reagent, it is possible to make a sufficiently satisfied differential diagnosis between the cancer and non-cancer urine.

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