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The Study of Possibility of Finding a Reagent for Cancer Diagnosis by Urine NMR Measurement

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═ **Abstract** ═

Cancer urine NMR measurement was previously made to find a possible method of differential diagnosis between cancer and non-cancer patients. It was found that there was the characteristic and common range of 3.00±0.06 ppm to 3.09±0.06 ppm appearing in the patients' urine. The signals were identified as the proton NMR frequency- signals of the NH compound elements of aromatic amines. It was found that the signals were caused by a substance of tyrosine. A reagent has recently been developed to identify the substance and to diagnose cancer by a urine color reaction. The reagent sensitivity and specificity obtained from a primary trial are respectively 79.2% and 75.0%.

1. INTRODUCTION

Urine NMR (Nuclear Magnetic Resonance)[1] experiments[2~5] have been performed to find a possible method of diagnosing cancer by discovering some common and characteristic proton NMR frequency-signals of cancer patients' urine rather than by closely analysing the composition of urine. It was found that the distributions of the NMR signals of the cancer patients' urine were quite different from those of the noncancer patients' and that there was the characteristic and common range of cancer urine NMR signals[2~5] of 3.00±0.06 ppm to 3.09±0.06 ppm* appearing in the urine only. The range was identified as the proton NMR signals of the NH compound elements of aromatic amines, and moreover recently it has been confirmed that the range is resulted from the substance of tyrosine[6,7] excreted in the urine after all.

In this paper, an attempt has been made to find a reagent which is possibly utilized for cancer diagnose by identifying the substance excreted in the urine. A primary test has bee made to determine the reagent sensitivity and specificity of 40 persons' urine obtained by a random sampling.

2. EXPERIMENT

A jellied reagent** is obtained by use of the Millon indicator and gelatin. One gram of the reagent is added to 1 c.c. of urine in a test tube to observe the urine color

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*Some exemplary NMR signal distributions are shown in Appendix Ⅰ.
**The reagent has officially been approved by the Korea Patent Bureau.

Table 1. Comparison of the results diagnosed by the reagent with those confirmed by a medical examination.

Urine number	Name of disease confirmed by a medical examination	Urine reaction	Urine number	Name of disease confirmed by a medical examination	Urine reaction
1	Stomach cancer	N	17	Pneumonia	N
2	Stomach cancer	P	24	Bronchitis	N
3	Stomach cancer	P	25	G-I bleeding	N
10	Stomach cancer	P	27	G-I bleeding	P
4	Hepatitis	N	33	Cholecystitis	N
5	Hepatitis	N	34	Gastritis	N
15	Hepatitis	N	38	Uterine cervix cancer(Ib)	P
7	Hepatoma	P	47	Endometrial cyst	N
32	Hepatoma	P	42	Endometritis	N
8	Lymphoma	P	51	Rhabdomyo sarcoma	P
9	Common bile duct cancer	P	54	Hepatoma	P
13	Pancreatic head cancer	N	53	Hepatoma	P
20	Rectal cancer	P	55	Hepatoma	P
30	Rectal cancer	P	43	Stomach cancer	P
18	Leukemia	P	59	Stomach cancer	P
23	Hypertensive heart disease	P	44	Stomach cancer	P
26	Diabetic mellitus	P	63	Stomach cancer	N
37	Cerebro vascular accident	N	61	Stomach cancer	N
39	Idiophothic heart disease	N	64	Stomach cancer	P
7	Pneumonia	N	65	Stomach cancer	P

N＝Negative(non-cancer), P＝Positive (cancer)

reaction. It is observed that the reagent reacts to cancer urine becomes red only. This phenomenon indicates that the urine contains the substance of tyrosine.

3. RESULTS AND DISCUSSION

By way of trial, a test is given to 40 person's urine obtained by a random sampling with the reagent in order to examine its sensitivity and specificity. The above table shows the comparison of the results diagnosed by the reagent with those confirmed by a medical examination. From the results of the urine reactions in Table 1 the reagent sensitivity and specificity are obtained respectively as follows:

$$\text{Sensitivity} = \frac{19}{19+5} = 79.2\%$$

$$\text{Specificity} = \frac{12}{4+12} = 75.0\%$$

Each urine number in the table is labelled by the Hanyang university hospital and the Saint Mary hospital in Seoul. N and P represent respectively negative reaction and positive reaction, and N indicates non-cancer and P cancer.

In conclusion although the above two results are nothing but such as obtained by one trial, it seems to suggest that the developed reagent will lead to the possibility of cancer diagnosis or rather to suggest that cancer urine contains a relatively higher concentration of the substances than-cancer urine. Fur-

Appendix I

The following figures of Figs. 1 to 6 show the exemplarly NMR signal distributions of cancer and normal urine:

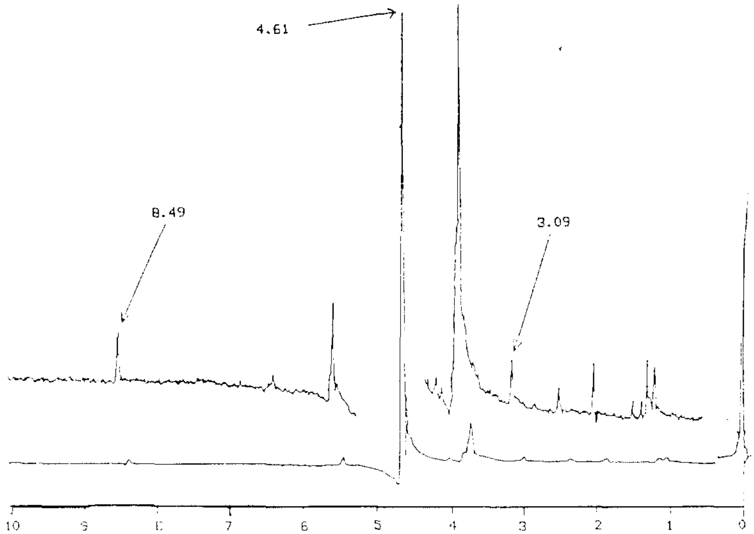

Fig. 1. Proton NMR signal distribution of the cervix cancer patient's urine observed by 100×1.5 of spectrum amplitude at room temperature.

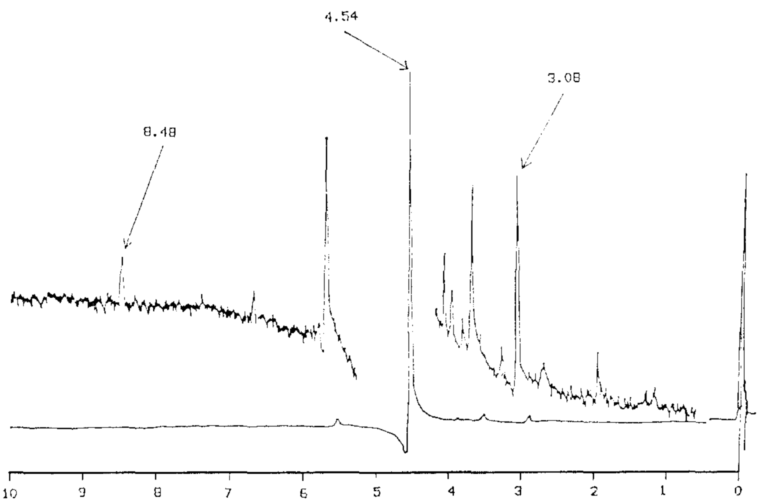

Fig. 2. Proton NMR signal distribution of the cervix cancer patient's urine observed by 100×8 of spectrum amplitude at room temperature.

It is noted that the particulary interested signals are revealed by numerals to demonstrate the NMR range stated earlier in the introductory remarks. The signals of 8.49±0.06 ppm, 8.48±0.06 ppm and 8.43±0.06 ppm on the extreme left-hand sides of the first three figures are caused by the anti-cancer agent of methotrexate medicated.

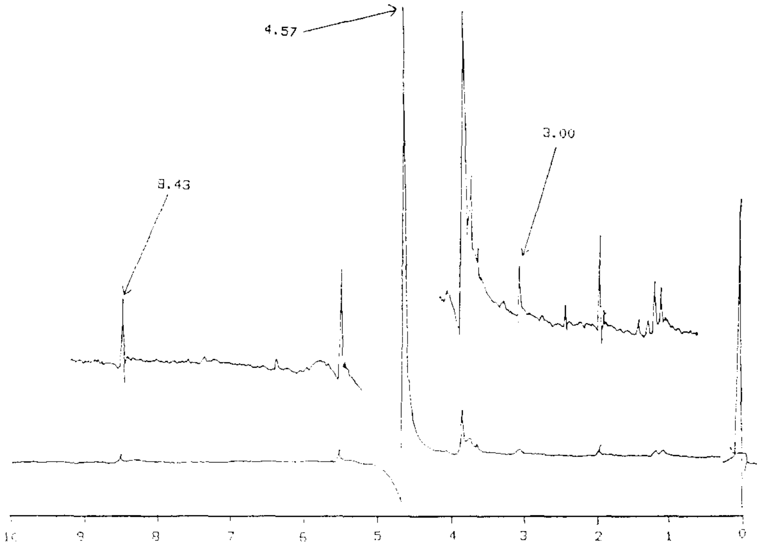

Fig. 3. Proton NMR signal distribution of the endomtrial cencer urine observed by 100×1 of spectrum amplitude at room temperature.

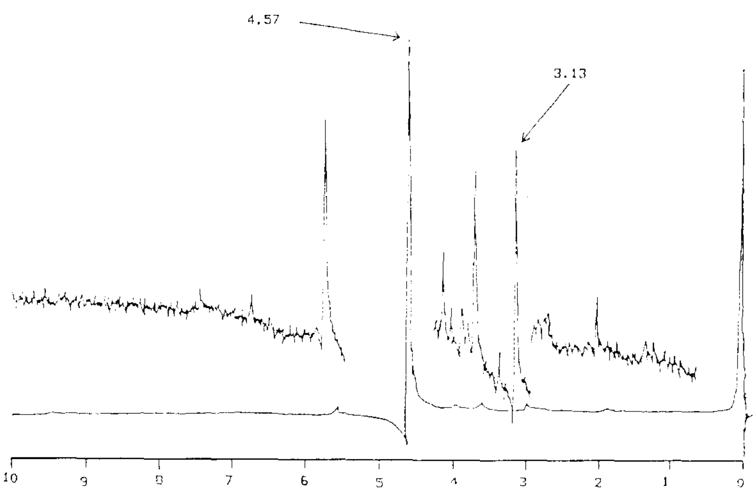

Fig. 4. Proton NMR signal distribution of the tubal pregnancy patient's urine observed by 100×8 of spectrum amplitude at room temperature.

ther experiments on the urine collected from a large number of people are in progress to determine the sensitivity and specificity more specisely for practical adoption by clinics.

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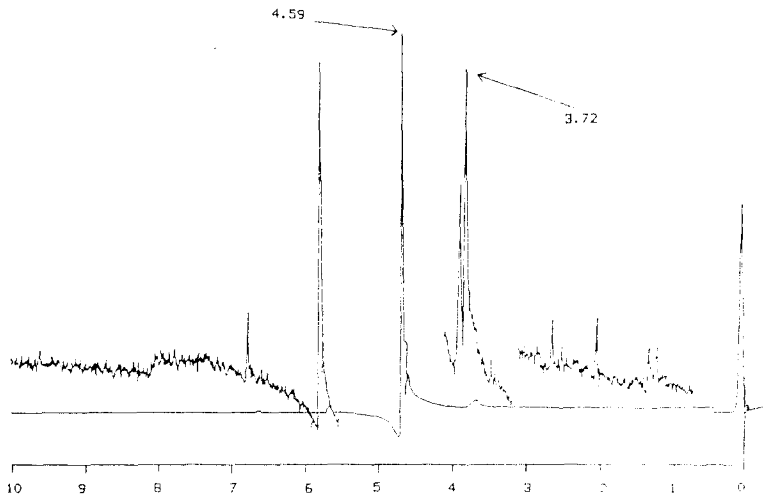

Fig. 5. Proton NMR signal distribution of the myoma patient's urine observed by 100×8 of sectrum amplitude at room temperature.

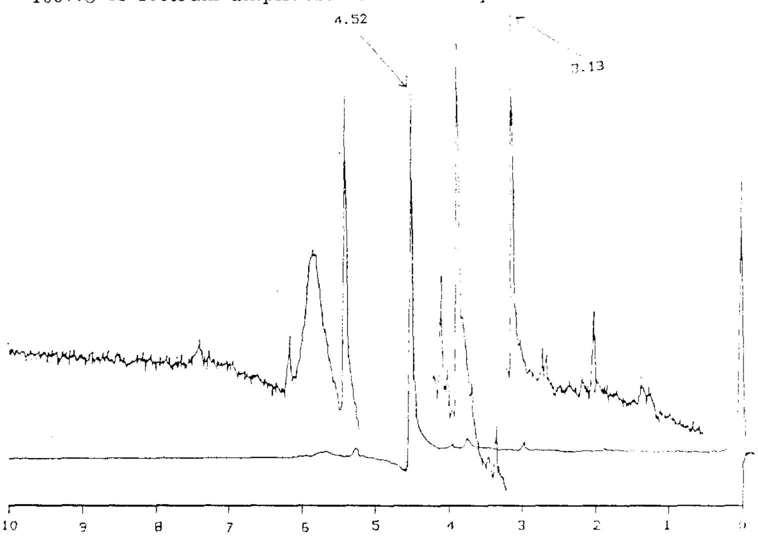

Fig. 6. Proton NMR signal distribution of the ectopic pregnancy patient's urine observed by 100×5 of spectrum amplitude at room temperature.

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