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https://doi.org/10.15017/7329575

出版情報：福岡醫學雜誌. 85 (8), pp.247-250, 1994-08-25. 福岡医学会
バージョン：
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# Liver Injury Induced by Dichloropropanols —Changes in the Time Course on Hematological and Blood Chemical Examinations—

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**Abstract** The toxicity of dichloropropanols (DCPs) was investigated by hematological and blood chemical examination. Solutions of two isomers of DCPs, 1, 3-dichloro-2-propanol (DC2P) and 2, 3-dichloro-1-propanol (DC1P) were dissolved in saline at a concentration of 100 mg/ml and 0.1 ml of each was subcutaneously injected into male Wistar rats weighing about 200 g. Acute changes on transaminases and number of platelets were determined in the time course. 6 hours later, transaminases showed significant increases while the number of platelets significantly decreased in the DC2P-treated group. In the half the of DC2P-treated group, transaminases had increased furthermore at 24 hours, while those in the rest were recovered to the control level. No changes were observed in the DC1P-treated group. These results indicate that there is a prominent hepatotoxicity in DC2P, with the individual diversities to some extent and the hepatic toxicity differs considerably between DC2P and DC1P. Therefore, the monitoring of the working environment and biological monitoring of DCPs should be mandatory, in the workplace where DCPs, especially DC2P, are utilized.

## Introduction

Dichloropropanols (DCPs) consisting of 1, 3-dichloro-2-propanol (DC2P) and 2, 3-dichloro-1-propanol (DC1P) are colorless viscous liquids with chloroform-like odor. They are used as solvents in hard resins and nitrocellulose in the manufacture of chemicals and lacquer, as cement for celluloid, or as binders for water colors[4]. Although acute toxicity induced by DCPs is assumed to be the same as that by carbon tetrachloride, including hepato-and nephrotoxicity, there are few reports concerning the toxicity of DCPs on humans and experimental animals.

Recently, we encountered several human cases of acute liver injuries due to the accidental exposure to DCPs[2][3]. We have already investigated the acute toxicity of DCPs with rats in the cross sectional study and revealed a prominent hepatotoxicity in DC2P and the different toxicity between DC2P and DC1P[1]. In this study, acute toxicities of DCPs were investigated by hematological and blood biochemical changes in the time course.

## Materials and Methods

Solutions of two isomers of DCPs, DC2P and DC1P, were dissolved in saline at a concentrations of 100 mg/ml, respectively and 0.1 ml of each was subcutaneously injected into male Wistar rats weighing about 200 g. The control rats were administered with an equal volume of saline. Eight animals of each group were sacrificed under deep ether anesthesia at 6, 24, and 72 hours after injection. Blood samples were obtained from the subclavian artery with ethylene diaminetetraacetic acid, dipotassium salt (EDTA-2K), as the anticoagulant for blood cell counts or heparin sodium salt for biochemi-

cal assays. Hematological examinations were carried out by A Towa Counter Analyzer and biochemical data such as glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) were assessed by a Hitachi Counter analyzer. Statistical significance ($P < 0.05$) was established by Wilcoxon 2-sample test.

## Results and Discussion

Laboratory data are shown in table 1 and figure 1. No changes were observed in laboratory findings in the DC1P-treated and control group at 6, 24 and 72 hours after DCPs injection. On the other hand, in the DC2P-treated group, the number of platelets decreased significantly at 6 and 24 hours and transaminases elevated extremely at 6 hours. In half of the DC2P-

**Table 1** Changes of platelet (PLT), GPT and GOT after DCPs treatment

| | | 6 h | 24 h | 72 h |
|---|---|---|---|---|
| PLT | control | 99.9±16.9 | 96.7±10.3 | 103.4±24.5 |
| | DC 1 P | 103.5±14.7 | 106.3± 9.6 | 107.1±22.7 |
| | DC 2 P | 13.8±10.2* | 49.1±38.4* | 92.9±27.4 |
| GPT | control | 25.9± 3.5 | 28.3± 3.2 | 19.0± 2.3 |
| | DC 1 P | 29.0± 6.0 | 24.0± 3.0 | 22.0± 3.0 |
| | DC 2 P | 697±621* | 1455±1999 | 34.0±25.0 |
| GOT | control | 73.9±15.3 | 93.5± 8.3 | 79.0±11.0 |
| | DC 1 P | 92.0±35.0 | 82.0±19.0 | 92.0±20.0 |
| | DC 2 P | 1735±946* | 6295±9233* | 122.0±88.0 |

The results are expressed as mean±SD of 8 rats
Significantly different from the control: *$P < 0.05$

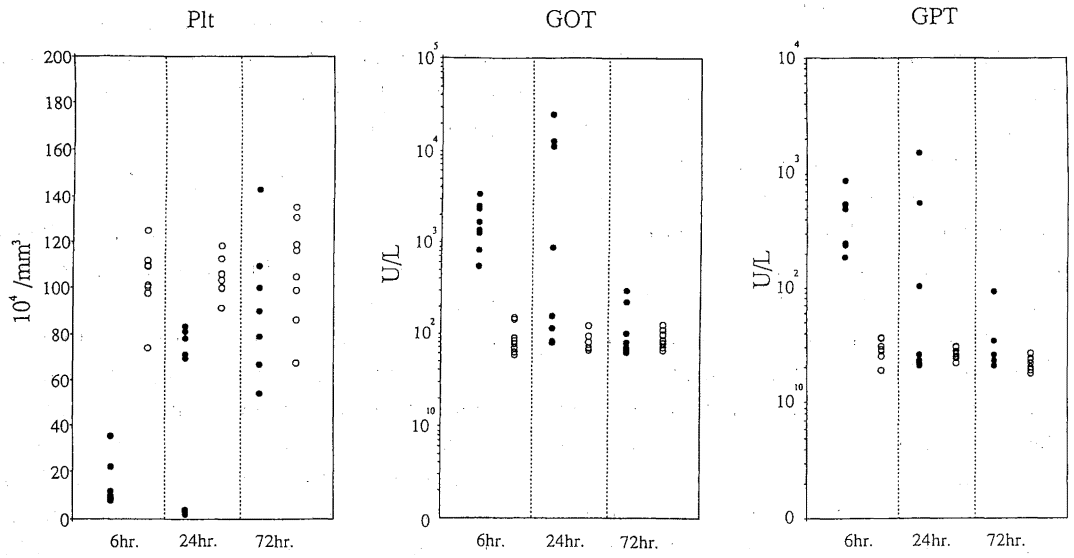


**Fig. 1** Changes of platelet count (Plt), glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) in the time course after 1, 3-dichloro-2-propanol (DC2P, closed circle) or 2, 3-dichloro-1-propanol (DC1P, open circle) injection.

treated group, transaminases had significantly increased, furthermore, at 24 hours, while those in the rest were returned to the same level as in the DC1P-treated and control groups. At 72hours after DC2P injection, transaminases and the number of platelets had been nearly recovered to the control level.

In the present study, acute hepatic toxicity of DCPs were clearly demonstrated. Moreover, serum alkaline phosphatase and lactate dehydrogenase did increase only in the DC2P-treated group at 6 hours. (data are not shown here) Thus, prominent hepatotoxicity was suggested to exist only in DC2P but its extent is different among individual animals. The toxicity of DC1P was not recognized in this experiment. There might be considerable differences in the hepatic toxicity between DC1P and DC2P. These findings reconfirmed our previous results about hepatic toxicity induced by DCPs[1]. This study may also show the reversibility of hepatic injuries induced by DCPs, since hematological and biochemical changes had been almost recovered to the normal range after 72 hours. The different manner of hepatic toxicity by two DCP isomers has not been well defined in our experiment. Further study should be conducted to clarify the mechanism of liver injury by DCPs. Our results indicate that the monitoring of the working environment and biological monitoring of DCPs should be recommended, in the workplace where DCPs, especially DC2P, are utilized.

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(Received for publication June 27, 1994)

(和文抄録)

# ジクロロプロパノールによる肝障害
## —血算値および血液生化学検査値の経時的変化—

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産業現場で使用され，近年中毒例が報告されたジクロロプロパノール (DCPs) の毒性を，ラットを用いて検討した．雄性ウィスター系ラットに，DCPs の 2 種の異性体である 1，3-ジクロロ-2-プロパノール (DC2P) および 2，3-ジクロロ-1-プロパノール (DC1P) を 100 mg/ml の濃度で生理食塩水に溶解させたものを，0.1 ml 皮下に投与した．DC2P 投与群では 6 時間後に血小板数は有意に低下し，血清トランスアミナーゼ値は有意に上昇した．これらの値は，24 時間後には，約半数において生理食塩水を投与した対照群と同レベルに戻り，残りの半数では，さらに上昇していた．DC1P 投与群では血小板数および血清トランスアミナーゼ値に変化は認めなかった．これらの結果は，ジクロロプロパノールの肝毒性について，DC2P と DC1P の 2 つの異性体間に著明な差があること，主として DC2P が急性肝毒性を示すが，その程度には個体差が存在することを示しており，ジクロロプロパノールの肝毒性についてさらに詳細に検討する必要があるものと考えられた．