# *The analytical consequence of the decomposition of prednisolone to 17-deoxyprednisolone in stability control*

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ABSTRACT

17-Deoxyprednisolone, a decomposition product of prednisolone, interferes in some stability-indicating spectrophotometric methods for corticosteroids. The false positive reaction of 17-deoxyprednisolone with tetrazolium blue and with the method of BUNDGAARD and HANSEN (1979), is discussed.

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The determination of corticosteroids with tetrazolium blue is well known. Many papers have been published dealing with this method (GÖRÖG and SZÁSZ 1978). It is known that this determination is possible for corticosteroids with a hydroxyl group or a hydrogen atom at C17 , e.g. CHEN *et al.* (1953) described the determination of hydrocortisone as well as corticosterone with tetrazolium blue. The determination of corticosteroids with tetrazolium blue is based on the oxidation of the hydroxyl group at C21 (Fig. 1A) of the $\alpha$-ketolic side chain (20-keto, 21-hydroxy), to an aldehyde group at C21 (Fig. 1B) and a reduction of tetrazolium blue to the blue coloured mono- and diformazans (GÖRÖG and HORVÁTH 1978).

In stability control many authors claim that the tetrazolium blue assay is specific for the intact dihydroxy-acetone side chain and neither the hydrolytic nor the oxidative decomposition products of the side chain react with tetrazolium blue and hence tetrazolium blue is used for the stability assay of corticosteroid preparations (ALLEN and DAS GUPTA 1974; BAUWENS and LOGGHE 1976; GÖRÖG and SZÁSZ 1978; GRAHAM *et al. 1970;* JENSEN and LAMB 1964; MAUGER *et al.* 1969).

During our own investigations on the stability of prednisolone (Fig. 1A, R=OH) under anaerobic conditions, one of the identified decomposition products was 17-deoxyprednisolone (Fig. 1A, R=H) (DEKKER 1979). Consequently the 17-deoxyprednisolone is also determined with tetrazolium blue. In our own investigations, a thin-layer chromatogram shows 17-deoxyprednisolone as a blue coloured spot with tetrazolium blue (DEKKER 1979).

BUNDGAARD (1978) and BUNDGAARD and HANSEN (1979) described a stability-indicating spectrophotometric method for the determination of corticosteroids with a dihydroxy-acetone side chain in aqueous media. This method is based on an oxidation of the C21 hydroxyl group to an aldehyde group with a cupric salt in an aqueous borate buffer solution and subsequent condensation with 3-methyl-benzothiazol-2-one-hydrazone in alkaline solution. It was likely, that this condensation with the aldehyde of 17-deoxyprednisolone was possible. Indeed a positive reaction was obtained. At 394 nm the relation between the specific absorbance of prednisolone and of 17-deoxyprednisolone was 10:3.5. Consequently to avoid the interference of 17-deoxyprednisolone, it is better to use a chromatographic separation previous to the tetrazolium blue method or the method of BUNDGAARD and HANSEN, in stability investigations of prednisolone.

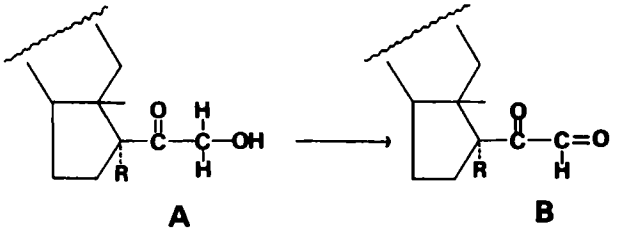


Fig. 1. The oxidation of the hydroxyl group at C21(A) to an aldehyde group (B)

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For other corticosteroids with a dihydroxyacetone side chain an analogous interference is likely.

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# *Determination of 8-methoxypsoralen in biological fluids by reverse phase* HPLC

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ABSTRACT

A sensitive HPLC-method is presented for the determination of 8-methoxypsoralen in body fluids. The method involves one single extraction with an organic solvent, chromatography on a reverse phase $C_{18}$ column and UV-detection at 254 nm.
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## INTRODUCTION

In recent years 8-methoxypsoralen (8-MOP) has been used in the treatment of psoriasis. The treatment consists of oral ingestion of 8-MOP, followed by irradiation with longwave ultra violet light (UV-A, 320-400 nm), it is called PUVA (Psoralen UV-A). Various analytical methods have been proposed for the quantitative determination of 8-MOP in biological fluids.

A spectrophotometric method (CHAKRABARTI *et al.* 1977) and determinations based upon gas liquid chromatography with flame ionisation detection, including thin-layer chromatographic clean up of the extracts (GAZITH and SCHAEFER 1977; WILKINSON and FARBER 1976), have been described. Both methods are not sensitive enough for measuring the low 8-MOP plasma levels (peak levels about 200 $\mu$g/l) reported in the literature. Methods based upon thin-layer chromatography followed by densitometry (CHAKRABARTI *et al.* 1978; HERFST *et al.* 1978) and gas liquid chromatography with electron capture detection (EHRSSON *et al.* 1977; SCHMID and KOSS 1978) are sufficiently sensitive, but time-consuming. High performance liquid chromatographic methods with a silica gel column (PUGLISI *et al.* 1977) and with a reverse phase CN-column (KREUTER and HIGUCHI 1979) have been described.

We developed a new HPLC method for the determination of 8-MOP. We chose a reverse phase $C_{18}$ column, that is widely used for the assay of many other drugs. The method is suitable for the routine assay of 8-MOP.

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