รายงานวิจัยฉบับสมบูรณ์

โครงการ การศึกษาการกระจายของยา ในระบบหมุนเวียนโลหิตของโพรงประสาทฟันหลังจากการกิน

Detection of Drug Distribution in Dental Pulp After Oral Administration

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กิตติกรรมประกาศ

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ให้คำปรึกษาทางด้าน Fluorescence Microscopy

ABSTRACT

Comparatively few studies have evaluated the distribution of drugs into human dental pulps of teeth with closed apices after oral administration. The objective of this study was to investigate whether or not tetracycline is distributed into dental pulp after oral administration. In the experimental group, patients were instructed to take tetracycline 500 mg after meals three times a day for two days prior to tooth extraction. Each extracted tooth was immediately sectioned and examined under ultraviolet light for the presence or absence of yellow fluorescence. Yellow fluorescence was found in all teeth in the experimental group. This was absent in the control teeth. It was also found in blood vessels of pulp chambers and root canals, and predentin lining the root canals. It is concluded that drug goes into human dental pulps of teeth with closed and opened apices after oral administration.

INTRODUCTION

The drug distribution in human dental pulps of mature teeth after oral administration has not been studied adequately. Tetracycline discoloration only demonstrates that drug goes into the dental pulp during early development of teeth, when the apices are still widely opened. It is well known that drugs are not distributed evenly into every tissue. Some do not enter the brain due to the blood-brain barrier (1). Some do not enter the eyes as a result of a blood-eye barrier (2). Dentistry has not used oral antibiotics to treat dental infection confined to the pulp tissue. It is of interest to note that there have been no studies showing that drugs are able to treat dental pulp infection. The objective of this study was to demonstrate whether or not drug could be seen in human dental pulps of teeth with closed and open apices after oral administration.

MATERIALS AND METHODS

Twenty-four permanent third molars and one premolar were used in the study. They were scheduled to be extracted as a result of orthodontic planning or reasons of, impaction or being the opposing teeth of the impacted ones. The configuration of the apical foramina was judged by x-ray and direct examination of the extracted teeth. Tetracycline hydrochloride was used as the index drug since it fluoresces under UV light at the wavelength of 270 nm (3). The subject ages ranged from 18- 25 years old, and none was pregnant as tetracycline HCl should not be given to pregnant women and children under 8 years old, since it will cause discoloration of teeth and bone, due to its propensity to bind to the

calcifying tissue (4). The study was approved by the ethic committee of Faculty of Dentistry, Chiang Mai University. Teeth in the experimental group were divided into 3 subgroups; 6 teeth with open apices, 11 teeth with closed apices, and 3 teeth with irreversible pulpitis. Five other teeth were used as controls. In the experiment group, patients were instructed to take tetracycline HCl 500 mg after meals 3 times a day for 2 days before tooth extraction. Three patients had history of taking tetracycline for the treatment of acne. Each extracted tooth was immediately sectioned and examined with naked eyes under ultraviolet light (Burton Wood lamp light) in a dark room for the presence or absence of yellow fluorescence of tetracycline HCl. A photograph of each tooth section was taken in a dark room, under UV light with magnifying glass, a Vivitar macro lens 105 mm, and x 2 teleadaptor.

RESULTS

Bright yellow fluorescence was demonstrated in all teeth in the experimental group, but not in the control group (Figs. 1a, 1b). Yellow fluorescent lines were observed in root dentin of teeth of the patients who had the history of taking tetracycline for the treatment of acne (Fig. 2b-3d). These lines are not the true result of this experiment.

Experimental group: Teeth with open apices

Teeth with open apices showed bright yellow fluorescence at the apical ends of the roots where active apical root formation and calcification were taking place (Figs. 1c-1h)

Experimental group: Teeth with closed Apices

Teeth with closed apices showed bright yellow fluorescence in the tissue of the pulp chambers, blood vessels, and root canals. Only large blood vessels appeared fluoresced. The predentin lining the pulp chambers also fluoresced (Figs. 2a-2g). Lines of tetracycline were observed in root dentin of the patients who previously took tetracycline for the treatment of acne (Fig. 2b, 2c). The yellow fluorescence in the pulp chambers of teeth with closed apices, interestingly, appeared brighter than that of teeth with open apices.

Experimental group: Teeth with Pulpitis

Three permanent third molars with closed apices affected with dental pulpitis showed remarkable results. Two of those with irreversible pulpitis showed an area of microabscess at the exposure area of the pulpal horn (Figs. 3a, 3c). Bright yellow fluorescence was seen in the tissue of dental pulp chambers, but not in the microabscess area (Figs. 3b, 3d).

DISCUSSION

Few studies have shown drug distribution from dental pulp to the blood stream after pulpotomy treatment (5,6). Tetracycline distribution from dental pulp into

periapical tissue and blood circulation has also been noted (7,8). There was an interesting study that found sulfanilamide and penicillin in the pulp fluid of dog following intramuscular and intravenous administration (9). It has also been found that pulp inflammation alters delivery of flurbiprofen to rat dental pulps (10). However there have been no studies showing that drugs enter the human dental pulps of teeth with fully formed apices after oral adminstration. In order to visualize the drug in dental pulps we used the fluorescence property of tetracycline, even though it is not the antibacterial of choice for dental pulp infection. Tetracycline not only stains bone and teeth after oral administration, but it can be detected in soft tissues as well. It has been used to detect cancer such as gastric carcinoma and osteosarcoma (4,11,12). Tetracycline has been reported to fluoresce under UV light in gingiva following the treatment of periodontitis with tetracycline impregnated fiber (13). An interesting study was carried out by Antalovski (1966) who injected rats with high dose of tetracycline intramuscularly. Tetracycline was found in the dentin of the incisors, but not that of the molars (14). This has raised the question if the distribution of drug into the dental pulp is tooth type-dependent or depends on stage of tooth development. Tetracycline discoloration of dentin in human teeth is an obvious evidence of drug going into the dental pulp, at the early stage of tooth development. Akimoto *et al.* (1985) reported the concentrations of ampicillin and talampicillin in the dental pulp of surgically removed permanent third molars (15,16). As the teeth were surgically splitted and removed, subsequently we are convinced that the drug in saliva and blood might have contaminated the dental pulp tissue (17).

We have demonstrated for the first time that drug goes into human dental pulp of teeth with closed apices after oral administration. In teeth with open apices, tetracycline appeared to localize in the apical region of the roots. However, in those with closed apices, the yellow fluorescence in the dental pulps appeared brighter than those of open apices. We hypothesize that the closed apexed-teeth are more suitable for carrying drug into the dental pulp chambers.

Teeth with irreversible pulpitis showed different brightness. We have demonstrated that tetracycline could reach the dental pulp chambers, but not the microabscess areas (Figs. 3b, 3d). This could be explained by the lack of blood supply in the necrotic areas of microabscess (18).

Our study has proved that after oral administration, drug enters into human dental pulps of teeth with either closed or open apices. Bright fluorescent predentin lining the pulp chambers indicates that blood circulation in the dental pulp is capable of transporting antibiotic to the mineralization front. Pharmacologically, we hypothesize that oral antibiotics of choice such as amoxicillin may be able to treat dental pulp infection. Further studies are needed to substantiate this hypothesis. Dental pulp cappings with calcium hydroxide do not usually have very successful results (19). Dental pulp cappings incorporated with oral antibiotics along with concurrent systemic antibiotic therapy may provide better result.

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Figure Legends.

Figs. 1 a) and b) Control teeth under UV light show no fluorescence. Experimental group. Teeth with open apices c) Molar with open apices. d) Tooth in c) under UV light. Note yellow fluorescence in the root canal and pulp chamber. e) - h) Yellow fluorescence in the tissue of pulp chambers, root canals, and the apical ends of the roots.

Figs. 2 Experimental group. Teeth with closed apices. a) Yellow fluorescence in the pulp chamber and root canal. Note yellow fluorescence in blood vessels. b) Bright yellow fluorescence in the dental pulp. Root dentin shows lines of previously taken tetracycline for treatment of acne. c)-g) Fluorescence in the pulp chambers and root canals.

Figs. 3 Experimental group. Molars with closed apices, affected with irreversible pulpitis. a) and c) Microabscess at the area of pulp exposure. b) Molar in a) and d) Molar in c) under UV light. Note yellow fluorescence in the pulp chambers and root canals, but not in the microabscess areas (arrows).

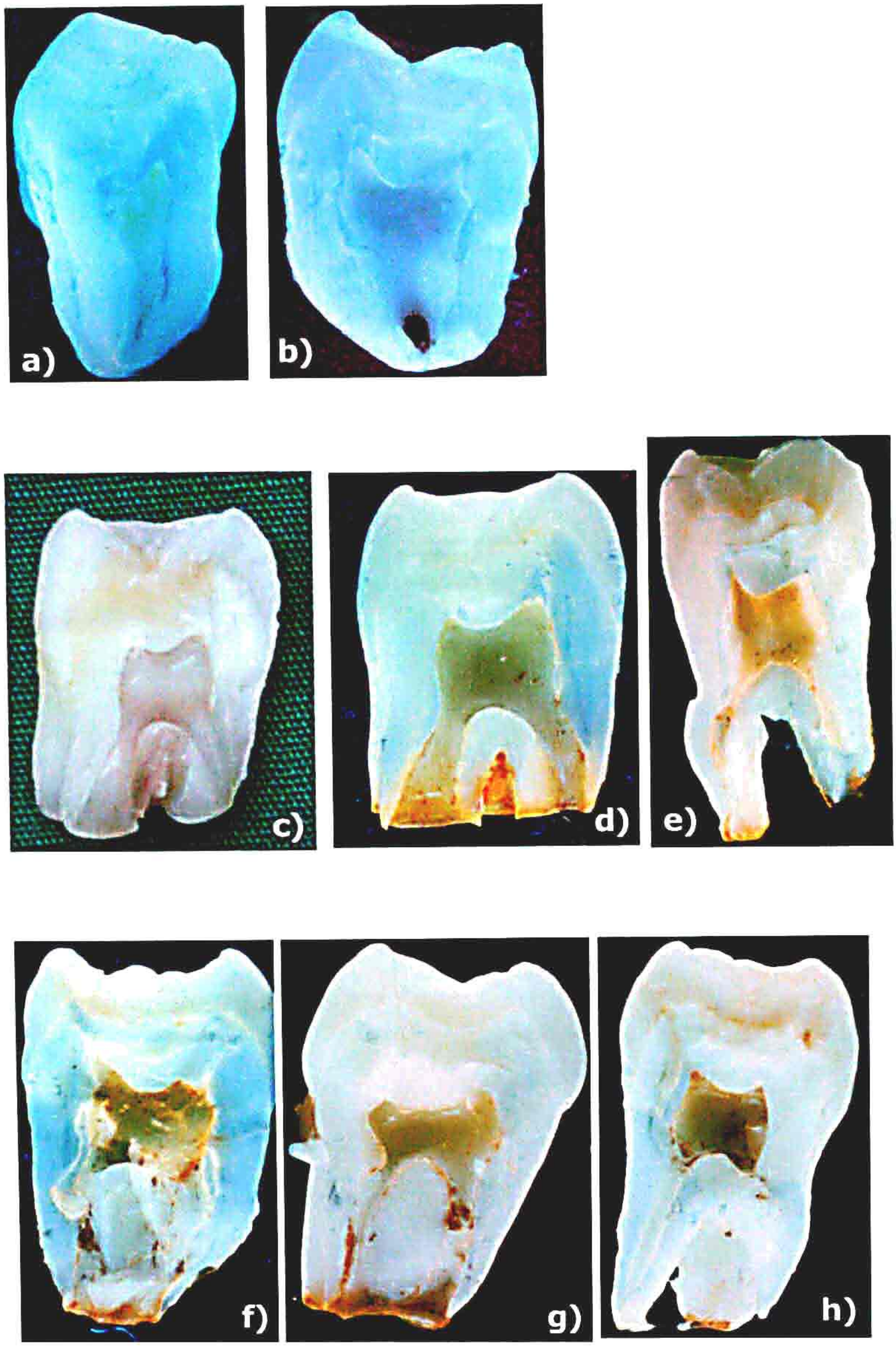

Fig. 1: Kantaputra et al. / Drug distribution in dental pulp

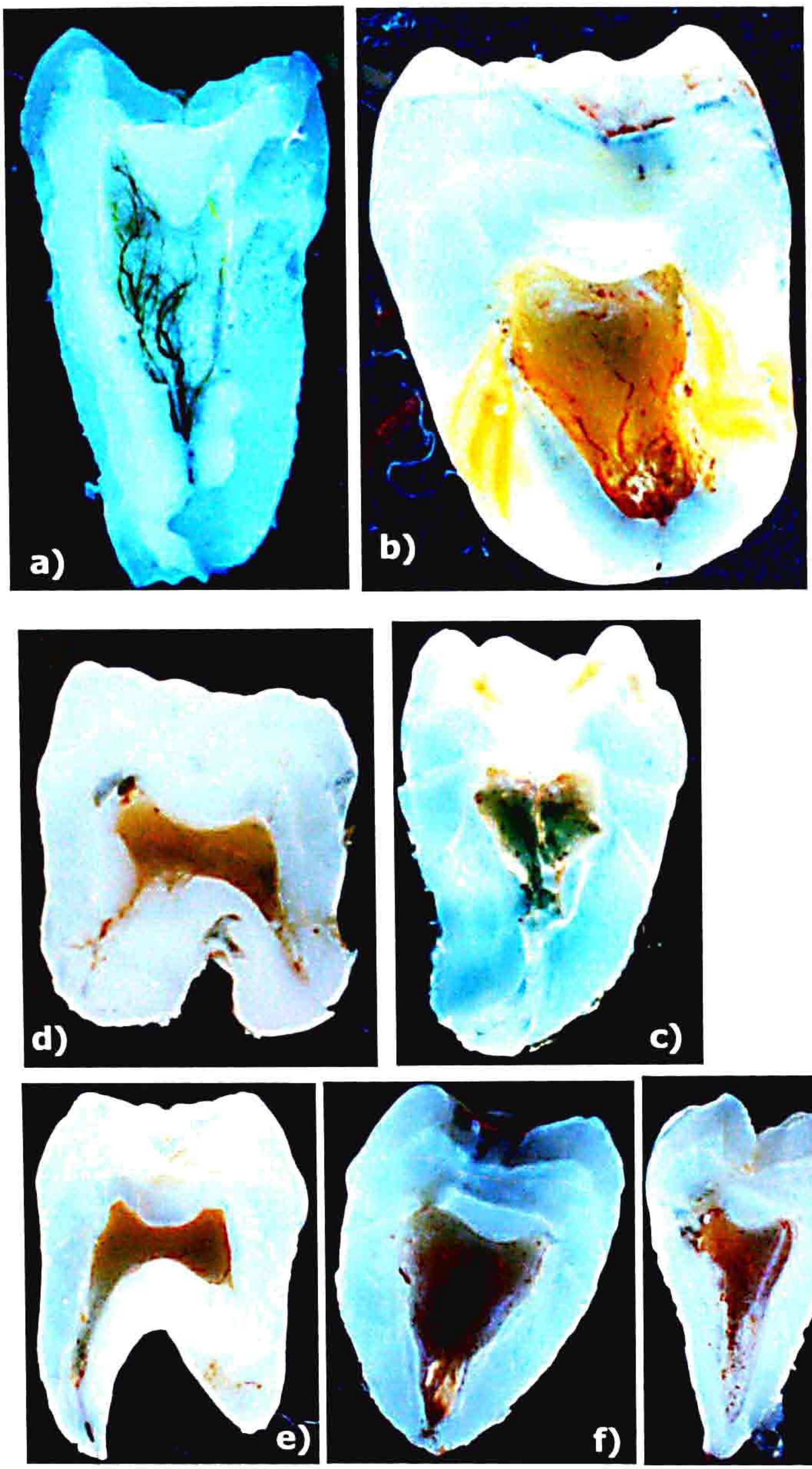

Fig. 2: **Kantaputra et al. / Drug distribution in dental pulp**

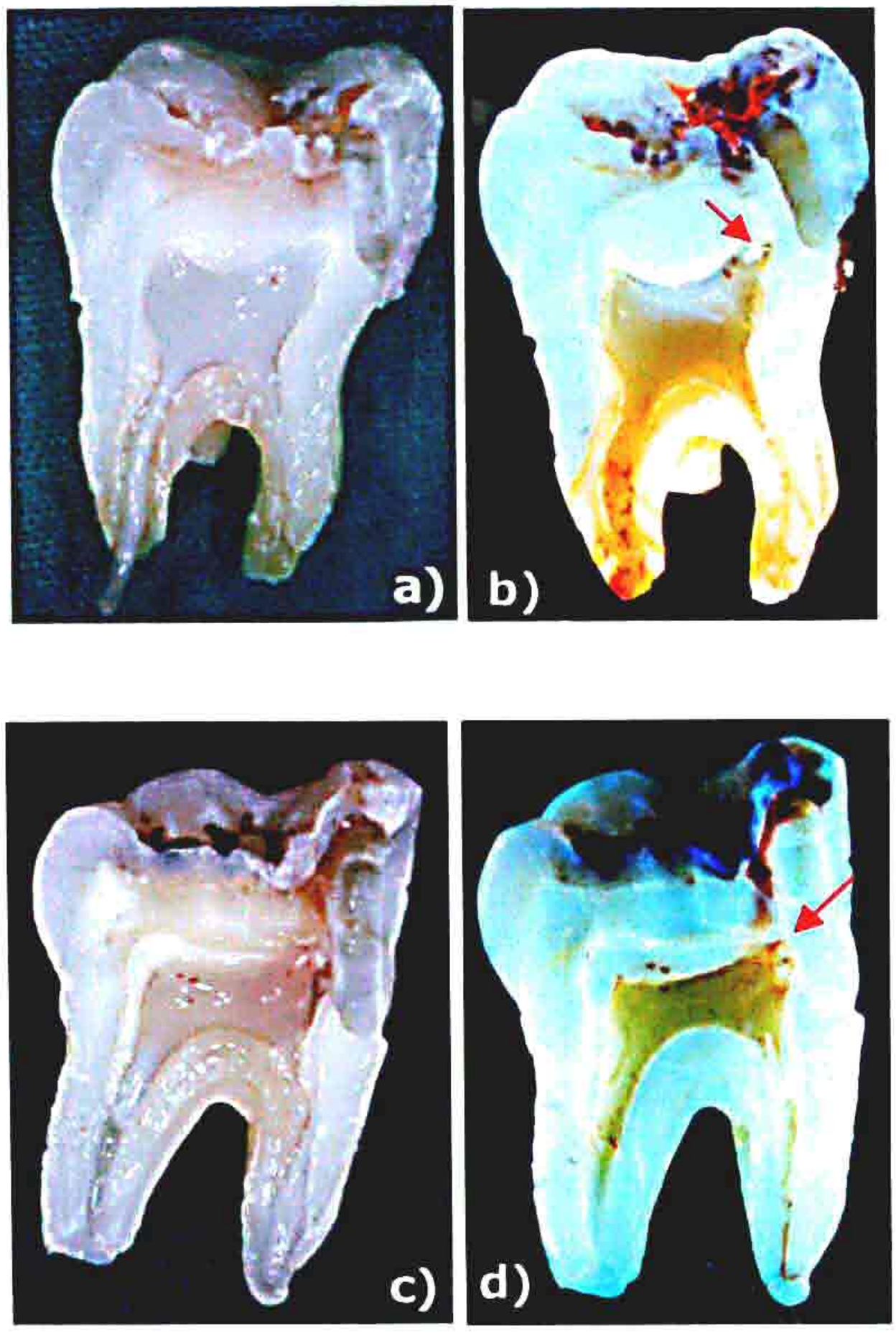

Fig. 3: Kantaputra et al. / Drug distribution in dental pulp