INTRODUCTION

INTRODUCTION

In the last two decades, medical oncology had become firmly established as a subspecialty of internal medicine *(Kennedy et al., 1977).*

In the 1960s many new antineoplstic drugs came into clinical use, and in subsequent years the emphasis has been on developing new combinations of available drugs, optimizing their timing and dosage, and modulating their toxicities *(Eilber et al., 1987).*

The proper application of new drugs requires knowledge of the mechanisms of action and metabolism of the drugs involved, as well as their effects on normal tissues *(Damon and Cadman, 1989).*

Cis-diamminedichloroplatinum II (Cisplatin), a widely used chemotherapeutic agent a divalent platinum compound and potent cell-cycle nonspecific chemotherapeutic agent, produces a dose limiting, permanent high frequency sensory-neural hearing loss and dose related cumulative renal insufficiency *(Campbell et al., 1996).*

Most recent interest has been centered on the ototoxic side effects of the first of a new antineoplastic drugs, Cis-platinum dimmine dichloride (Cis-DDP). It is a cytotoxic agent which is being increasingly used in the management of pediatric solid tumours. It has contributed to improve response rates in osteosarcoma and germ cell tumours *(Pinkerton et al., 1986).* Some studies have highlighted its efficacy in certain resistant malignancies such as neuroblastoma, and its apparently greater efficacy when used in higher dose regimens *(Dini et al., 1987).*

However, its recognised side-effects include ototoxicity, nephrotoxicity and myelosuppression. Renal damage is the major dose-limiting toxicity, but this has been reduced by improved methods of administration *(Skinner et al., 1990).*

The biologic activity of platinum coordinate compound was first recognised in 1965, when Rosenberg and Colleagues observed inhibition of cell division of E-coli, near a platinum electrode. After attempts to explain this phenomenon, those investigators subsequently isolated a metal complex, Cisplatinum, which has become the model for a new class of therapeutic compounds *(Loehrer and Einhorn, 1984).*

The exact mechanism (s) of ototoxicity and/or nephrotoxicity of cisplatin are still unknown. Continued aggressive high-dose cisplatin chemotherapy necessitates the investigation of ways to decrease the dose-limiting side effects that inhibit the administration of cisplatin at therapeutic and tumoricidal doses *(Schweitzer, 1993).*

The pharmacokinetics of cisplatin were compared with those of caboplatin. The perilymphatic concentration of carboplatin was one seventh of that of cisplatin even 1 hour after the administration *(Sato et al., 1995).*

The commonly used method of preparing the temporal bone for light microscopy is refinement of a basic formula that has been empolyed for a century. This process includes fixation, decalcification, neutralization, dehydration, embedding in celloidin, and hardening. The main disadvantage of this process is that declacification which performed

prior to sectioning prevents accurate quantitative evaluation of specimen *Schuknecht (1993).*

New technique for preparing undecalcified bone sections have been developed by embedding temporal bones in Methyl- Methacrylate *(Benny et al., 1995).*

The main advantage of this new method is that no decalcification is involved, so that all bony elements are retained in their normal shape and location, and even retain some enzymatic activity. Other advantages are that the fixation is reversible and the process is short (approximately 2 weeks) *(Benny et al., 1995).*