

Cutaneous Toxicity and Absorption of Paraquat in Porcine Skin¹

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Paraquat, a commonly used herbicide, has been shown to be toxic in exposed field workers. The objectives of this study were to (a) assess the cutaneous toxicity of paraquat *in vivo* in pig skin and *in vitro* in the isolated perfused porcine skin flap (IPPSF) and (b) quantitate its absorption in the IPPSF. The amounts of 3, 24, and 200 mg of paraquat were topically applied (5 cm² surface area) on the ventral abdomen of pigs and biopsied after 6-8 hr for light microscopy (LM) and transmission electron microscopy (TEM). IPPSFs were topically dosed with the same concentrations and perfused for 8 hr ($n = 4/\text{treatment}$). The dosed area of the skin was sampled for LM, TEM, and enzyme histochemistry. IPPSFs were also treated topically with [¹⁴C]paraquat dichloride at the aforementioned concentrations ($n = 4/\text{dose}$) and hourly perfusate samples were collected for radiolabel determination and assessment of biochemical and physiological parameters. The epidermal changes were similar both *in vivo* and *in vitro*. The changes included epidermal intercellular edema which increased with dose and epidermal-dermal separation at the 200-mg dose. Acid phosphatase and nonspecific esterase activities were increased in the upper layers of the epidermis, while alkaline phosphatase showed a greater activity in the stratum basale layer. Glucose utilization of all treated IPPSFs was lower than that of the controls and a variation in the vascular resistance profiles was seen in all the treated flaps. Radiotracer studies indicated that a majority of the compound remained on top of the application site and minimal absorption or penetration into skin was observed. Thus, at high concentrations and prolonged exposure, paraquat may have deleterious effects on epidermal morphology in the absence of significant percutaneous absorption. © 1992 Academic Press, Inc.

Paraquat (1,1'-dimethyl-4,4'-bipyridinium dichloride) is a contact herbicide which is widely used in the agricultural industry to aid in the harvesting of a wide variety of crops. Approximately 5×10^6 hectares are sprayed annually with paraquat in Europe alone (Sagar, 1987). Its widespread use

stems from its usefulness as an effective nonselective weed eliminator (kills a wide variety of monocots and dicots). Paraquat was first introduced in Great Britain in 1962 and became commercially available in the United States in 1964. It is a hydrophilic compound available in granular and liquid forms (Kimbrough, 1974). Paraquat is a permanently charged cation and is dissociated at all pH values (Clark *et al.*, 1966). Its contact herbicidal properties have advantages over other foliage-applied translocated herbicides. The major environmental concern of pesticide/herbicide residue is not of significance in the use of paraquat since it is easily inactivated upon contact with soil or sunlight. Despite its usefulness, paraquat is a well-known lung, nail, and ocular toxicant (Cant and Lewis, 1968; Samman and Johnston, 1969). The major cause of systemic toxicity leading to death is accidental oral ingestion.

The systemic effects and the mechanisms of action have been well studied (Clejan and Cederbaum, 1989; Rosen *et al.*, 1989). Paraquat is a potent free radical generator (Juchau *et al.*, 1986) and is actively accumulated by various tissues such as lung and brain. It competes with natural oligoamines in the body for its uptake and accumulation (Nemery *et al.*, 1987; Wyatt *et al.*, 1988).

There have been relatively few cases of fatality due to dermal exposure of paraquat (Smith, 1988; Athanasielis *et al.*, 1983; Tungsanga *et al.*, 1983). Even though various dermal absorption studies have been conducted (Chui *et al.*, 1988; Dey *et al.*, 1990; Scott *et al.*, 1986; Tabak *et al.*, 1990), and clinical cases of dermal necrosis have been reported, there is a dearth of information regarding detailed morphological changes seen upon topical exposure through skin.

It is well documented that porcine skin closely resembles human skin both structurally and functionally, and the isolated perfused porcine skin flap (IPPSF) has been proven to be a useful alternative *in vitro* model for the study of direct cutaneous toxicity (King and Monteiro-Riviere, 1990; Riviere *et al.*, 1986; Monteiro-Riviere *et al.*, 1987; Monteiro-Riviere, 1990b). Topical absorption, penetration, and quantification of various chemicals and drugs have been extensively studied and the results have shown an excellent correlation to human studies and other *in vivo* situations (Carver *et al.*, 1989; Williams *et al.*, 1990; Riviere and Monteiro-Riviere, 1991). It is, therefore, the objective of this paper to describe the morphological changes seen upon top-

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Cutaneous Toxicity

Adolph Rostenberg, Frederick Coulston

Cutaneous Toxicity:

Principles of Toxicology Testing Frank A. Barile,2007-07-23 The evolution of toxicology testing finds its impetus in the continuing growth of the chemical and pharmaceutical industries as well as the awareness of public health initiatives needs and responses that demand faster more accurate more economical methods for screening potential toxicity Concurrent advances in biotechnology enable viable in v *Cutaneous Toxicity* Victor Alexander Drill,Paul Lazar,1977 [Cutaneous Toxicity](#) ,1965 **Cutaneous Toxicity** Victor A. Drill,1977 **Veterinary Toxicology** Ramesh C Gupta,2011-04-28

Veterinary Toxicology 2nd edition is a unique single reference that teaches the basic principles of veterinary toxicology and builds upon these principles to offer an essential clinical resource for those practicing in the field This reference book is thoroughly updated with new chapters and the latest coverage of topics that are essential to research veterinary toxicologists students professors clinicians and environmentalists Key areas include melamine and cyanuric acid toxicogenomics veterinary medical geology toxic gases toxicity and safety evaluation of new veterinary pharmaceuticals and much more The 2nd edition of this popular book represents the collective wisdom of leading contributors worldwide and continues to fill an undeniable need in the literature relating to veterinary toxicology New chapters covering important and timely topics such as melamine and cyanuric acid toxicogenomics toxic gases and veterinary medical geology Expanded look at international topics such as epidemiology of animal poisonings regulatory guidelines and poisonous plants in Europe Heavily contributed book with chapters written by qualified and well experienced authorities across all areas of veterinary toxicology Problem solving strategies are offered for treatment as well as in depth knowledge of the basic mechanisms of veterinary toxicology

[Cutaneous Toxicity](#) Victor Alexander Drill,Paul Lazar,1984 *Haschek and Rousseaux's Handbook of Toxicologic Pathology Volume 5: Toxicologic Pathology of Organ Systems* Wanda M Haschek,Colin G. Rousseaux,Matthew A. Wallig,Brad Bolon,2025-02-09 *Haschek and Rousseaux s Handbook of Toxicologic Pathology* is a key reference on the integration of structure and functional changes in tissues associated with the response to pharmaceuticals chemicals and biologics Volume 5 of the Fourth Edition continues coverage of Organ Specific Toxicologic Pathology and major organ systems not covered in Volume 4 Completely revised Volume 5 of the Handbook of Toxicologic Pathology is an essential part of the most authoritative reference on toxicologic pathology for pathologists toxicologists research scientists and regulators studying and making decisions on drugs biologics medical devices and other chemicals including agrochemicals and environmental contaminants Includes completely revised chapters on systems toxicologic pathology Offers high quality and trusted content in a multi contributed work written by leading international authorities in all areas of toxicologic pathology Features hundreds of full color images in both the print and electronic versions of the book to highlight difficult concepts with clear illustrations **Current Concepts in Cutaneous Toxicity** Victor Alexander Drill,Paul Lazar,1980-01-01

Fundamentals of Toxicologic Pathology Matthew A. Wallig,Brad Bolon,Wanda M Haschek,Colin G.

Rousseaux,2017-10-25 Fundamentals of Toxicologic Pathology Third Edition presents an essential overview of systems toxicologic pathology in a clear and concise manner Toxicologic pathology integrates toxicology and its interdisciplinary components including biochemistry pharmacodynamics and risk assessment to pathology and its related disciplines such as physiology microbiology immunology and molecular biology This wholly revised and updated edition presents the newest information on the topic and is an essential reference for advanced students early career researchers toxicologic pathologists pharmaceutical scientists medical pathologists and clinicians and anyone involved with drug and device development The book includes a new section describing the application of toxicologic pathology such as diagnostic and forensic toxicologic pathology environmental toxicologic pathology experimental and industrial toxicologic pathology and pathology issues in the design of toxicology studies There are also new chapters on special senses the eye and ear and the biochemical and molecular basis of toxicity among others Presents revised and updated information for each chapter on systems Contains expanded sections on applied toxicologic pathology Includes the essential information necessary to understand toxicologic pathology in an accessible language

The Urologic and Cutaneous Review ,1917 [Journal of Cutaneous Diseases Including Syphilis](#) ,1917 **The Journal of Cutaneous Diseases Including Syphilis ...** ,1917 **Histopathology of Preclinical Toxicity Studies** Peter Greaves,1990 Histopathological assessment of tissue sections is an important component of many preclinical studies which are conducted to support the safety and clinical development of novel therapeutic agents for use in the treatment of human diseases The drug discovery process aided by modern biotechnology is now capable of generating highly potent pharmacologically active agents which can give rise to quite unusual constellations of tissue pathology The complexity and the number of histopathological findings in individual studies indicate the need for lucidity in descriptions and conclusions In the light of these and other difficulties this text is aimed towards bringing together into one volume a description of histopathological changes which relate to toxicity testing of therapeutic agents in the usual test species rat mouse dog and non human primate This book is an excellent starting point for the analysis of drug induced findings in toxicity studies

Archives of Dermatology and Syphilology ,1922 [Short-Term Toxicity Tests for Non-Genotoxic Effects](#) International Council of Scientific Unions. Scientific Committee on Problems of the Environment,1990-06-14 Presents the results of in vitro studies on cell cultures involving primarily undifferentiated cells systematic examination of the function of organs and the hematopoietic immunologic reproductive and other systems Identifies experimental approaches to supplement classical in vivo methods for determining the adverse effects of chemicals

Toxicological Profile for Pyrethrins and Pyrethroids ,2003 **Cutaneous Toxicity** Adolph Rostenberg,Frederick Coulston,1964 *American Journal of Diseases of Children* ,1928 **Toxicological Profile for Chromium** ,2000

Current Concepts in cutaneous toxicity ,1980

The Enigmatic Realm of **Cutaneous Toxicity**: Unleashing the Language is Inner Magic

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