

Luminol
[521-31-3]

Review of Toxicological Literature

Prepared for

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EXECUTIVE SUMMARY

The nomination of luminol by a private individual to the ICCEC is based on the lack of sufficient toxicological data and on the potential for human exposure.

Luminol is synthesized via cyclocondensation of 3-nitrophthalic acid with hydrazine in the presence of triethylene glycol. The product, 5-nitro-1,4(2*H*,4*H*)phthalazinedione, is then heated with sodium dithionite, treated with acetic acid, and cooled. In the process, the nitro group is reduced to an amino group. Luminol was produced by Kodak Corporation in the late 1970s. Current data on producers and production and import volumes were not available.

The ability of luminol to emit light (chemiluminescence) upon oxidation enables it to be used in assays to detect the presence of a number of inorganic and organic species (e.g., metal ions, hydrogen peroxide, nitrate, some alcohols, amines, amino acids, carbohydrates, cyanides, enzymes and enzyme substrates, and vitamins). Luminol-enhanced chemiluminescence probes have been used to quantify and characterize the secretion of oxygen by phagocytosing cells.

Luminol is currently used by most police agencies in the U.S. as a forensic tool for the detection of trace blood patterns at crime scenes; it is applied as an aerosol in a mixture with sodium perborate, sodium carbonate, and distilled water.

In limited clinical trials in the 1960s, luminol was used for the treatment of the patches of baldness caused by alopecia areata (an autoimmune disease), for the treatment of fluid accumulation in tissues of chronically ill patients, and for the promotion of blood clotting and wound healing. No adverse or toxic side effects were observed. There is no evidence, however, that it is currently used as a therapeutic agent. Luminol has never been approved for marketing by the FDA.

Law enforcement workers may be exposed to luminol during its use as a forensic tool for the detection of trace blood patterns at crime. Other workers may be exposed to luminol and its metabolite 3-aminophthalic acid while using it to conduct biochemical assays. No data were available on the number of workers exposed to luminol.

In vitro, the chemiluminescence-producing oxidation of luminol by the enzyme horseradish peroxidase yields three metabolites, one of which is 3-aminophthalic acid. The other two metabolites were not identified. Luminol binds to human serum albumin *in vitro*.

The oral LD₅₀ for luminol in rats was >500 mg/kg (>2.82 mmol/kg). Increased excretion of urine (diuresis) and sodium (natriuresis), and decreased arterial blood pressure were observed in female dogs following intravenous (i.v.) injection of a single dose of 2.5 mg (0.014 mmol) luminol (duration of observation period was not specified). No adverse effects were observed in mice injected intraperitoneally (i.p.) with a single dose of 1 to 5 mg (0.006 to 0.03 mmol) luminol and observed for 4 weeks.

Luminol was negative *in vitro* for the induction of gene mutations in *Salmonella typhimurium*, with or without metabolic activation, and in *Escherichia coli*, without metabolic activation. Luminol, at doses of 250, 500, and 1000 µM, greatly enhanced the frequency of SCE

in Chinese hamster V79 cells *in vitro*, but only when treatment occurred during S-phase in the presence of bromodeoxyuridine. It inhibited repair of DNA damage induced by methyl methanesulfonate (MMS) in Chinese hamster ovary cells, but had no apparent effect on UV-induced strand breaks. Luminol was reported to increase the efficiency of intrachromosomal homologous recombination in Chinese hamster A238 cells, and to affect the rate of single DNA exchanges and gene conversion (double exchanges) in LMtk⁻ and HeLa cells, respectively, which were transformed with plasmid DNA.

Luminol was reported to inhibit poly(ADP-ribose) polymerase, with greater efficiency than 3-aminobenzamide. As with other inhibitors, treatment of oncogene-transformed NIH-3T3 cells with luminol (250, 1000 µM) for 12 days after plating resulted in the marked appearance of flat cells, possibly by eliminating exogenous transforming genes, suppressed G₁ arrest and enhanced G₂ arrest in gamma-irradiated mouse embryonic fibroblast C3D2F1 3T3-a cells. It inhibited slow and fast potentially lethal damage (PLD) repair in x-ray irradiated V79 cells.

In rats, luminol (2 or 6%/kg feed; 110 or 340 mmol/kg feed) administered for 10 weeks starting 2 weeks after a single intraperitoneal (i.p.) injection of 200 mg/kg *N*-nitrosodiethylamine (DEN) did not affect the average liver weight or the development of liver foci. However, luminol at concentrations of 3 or 6%/kg feed (170 or 340 mmol/kg feed), administered concurrently with 0.05% (2 mmol) phenobarbital in the diet for 10 weeks following injection of 200 mg/kg DEN inhibited phenobarbital-dependent liver enlargement and development of glutathione *S*-transferase placental (GST-P)-positive liver foci. Luminol exerted no effect at the 1% or 2% level (56 or 110 mmol/kg feed).

A number of 2,3-dihydrophthalazine-1,4-dione derivatives possess anti-neoplastic activity *in vitro*. Of 28 derivatives tested (luminol was not included), most demonstrated potent cytotoxicity towards murine leukemia and human tumor cell lines. Only some of the tested derivatives, however, were active against *in vitro* growth of bronchogenic lung, osteosarcoma, and glioma cell lines.

No short-term, subchronic, chronic, reproductive, or carcinogenicity data were available.

TABLE OF CONTENTS

1.0	BASIS FOR NOMINATION TO THE ICCEC.....	1
2.0	CHEMICAL PROPERTIES.....	1
2.1	Chemical Identification.....	1
2.2	Physical-Chemical Properties.....	1
2.3	Purity and Commercial Availability.....	2
3.0	COMMERCIAL PRODUCTION PROCESSES.....	2
4.0	PRODUCTION AND IMPORT VOLUMES.....	2
5.0	USES.....	2
6.0	ENVIRONMENTAL OCCURRENCE.....	3
7.0	HUMAN EXPOSURE.....	3
8.0	REGULATORY STATUS.....	3
9.0	TOXICOLOGICAL DATA.....	4
9.1	General Toxicology.....	5
9.1.1	Human Data.....	5
9.1.2	Chemiluminescence.....	5
9.1.3	Metabolism.....	5
9.1.4	Acute Exposures.....	5
9.1.4.1	Intravenous Injection.....	6
9.1.4.2	Intraperitoneal Injection.....	6
9.1.5	Short-Term and Subchronic Exposures.....	8
9.1.6	Chronic Exposures.....	8
9.2	Reproduction and Development.....	8
9.3	Carcinogenicity.....	8
9.4	Genotoxicity.....	8
9.4.1	Prokaryotic Systems.....	8
9.4.2	<i>In Vitro</i> Mammalian DNA Damage.....	8
9.5	Other Toxic Effects.....	10
9.5.1	Effects on Enzyme Activity.....	10
9.5.2	Promotion of Liver Foci.....	10
10.0	STRUCTURE-ACTIVITY RELATIONSHIPS.....	11
11.0	ONLINE DATABASES AND SECONDARY REFERENCES.....	11

11.1	Online Databases.....	11
11.2	Secondary References.....	13
12.0	REFERENCES.....	13
	ACKNOWLEDGMENTS.....	16

TABLES

Table 1	LD ₅₀ Values for Luminol.....	6
Table 2	Acute Toxicity of Luminol.....	7
Table 3	Genotoxicity of Luminol.....	9

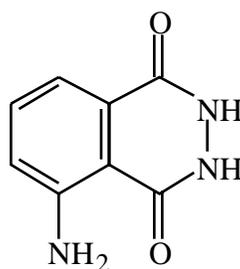
1.0 BASIS FOR NOMINATION TO THE ICCEC

The nomination of luminol [521-31-3] by a private individual to the ICCEC is based on the lack of sufficient toxicological data, and on the potential for human exposure.

2.0 CHEMICAL PROPERTIES

Luminol

[521-31-3]



2.1 Chemical Identification

Luminol (C₈H₇N₃O₂, mol. wt. = 177.16) is also called:

5-Amino-2,3-dihydro-1,4-phthalazine-dione
o-Aminophthalylhydrazide
 3-Aminophthalic hydrazide
o-Aminophthaloyl hydrazide

2.2 Physical-Chemical Properties

Property	Information	Reference
Color	White to yellow	MDL Info. Serv. (1994)
Physical State	Crystalline solid	Budavari (1996)
Melting Point, °C	319-320	MDL Info. Serv. (1994); Budavari (1996)
Specific Gravity	Approx. 0.90-1.0	MDL Info. Serv. (1994)
Dissociation Constant:		

Property	Information	Reference
pKa ₂	15.1	Haapakka et al. (1982)
Solubility:		
Water at 20°C	Soluble	MDL Info. Serv. (1994)
Organic Solvents	Soluble in alcohol	MDL Info. Serv. (1994)

Luminol is a slight fire hazard when exposed to heat or flame; it may form flammable or explosive dust-air mixtures. Thermal decomposition products may include toxic oxides of carbon and nitrogen (MDL Info. Serv., 1994).

Oxidation of luminol is accompanied by a striking emission of light (Budavari, 1996).

2.3 Purity and Commercial Availability

Commercially available luminols have been found to contain up to 11 contaminants (concentrations not provided), including 3-aminophthalimide (Stott and Kricka, 1987). The identities of the other contaminants were not provided in the abstract examined.

3.0 COMMERCIAL PRODUCTION PROCESSES

Luminol synthesis via cyclocondensation of 3-nitrophthalic acid with hydrazine in the presence of triethylene glycol was described recently by Nenzel (1995). The product, 5-nitro-1,4(2*H*,4*H*)phthalazinedione was then heated with sodium dithionite, treated with acetic acid, and cooled to yield luminol. In the process, the nitro group is reduced to an amino group. The preparation is similar to that briefly described for laboratory preparations reported in 1934, 1949, and 1964 (Budavari, 1996).

4.0 PRODUCTION AND IMPORT VOLUMES

Luminol was produced by Kodak Corporation in the late 1970s (TSCAPP, 1983). Current data on producers and production and import volumes were not available. Sources investigated included the U.S. ITC statistical reports, the *SRI Directory of Chemical Producers*, and the online version of STN International's *Chemical Economics Handbook*.

5.0 USES

The ability of luminol to emit light (chemiluminescence) upon oxidation (for reviews see Briheim et al., 1984; Radi et al., 1993; Lundqvist and Dahlgren, 1996) enables it to be used in assays to detect the presence of a number of inorganic and organic species. Luminol is used for the detection of metal ions, hydrogen peroxide, nitrate, some alcohols, amines, amino acids, carbohydrates, cyanides, enzymes and enzyme substrates, and vitamins (Bowie et al., 1996; Budavari, 1996).

Luminol-enhanced chemiluminescence probes have been used to quantify and characterize the secretion of oxygen by phagocytosing cells (Kahl et al., 1987). For example, luminol-enhanced chemiluminescence have also been used in assays to investigate the role of granulocyte-derived reactive oxygen species in damage to heart muscle, to monitor polymorphonuclear leukocyte function in patients with diabetes mellitus, the activation of leukocytes in patients with peritonitis, the release of interleukin-8, interleukin-6, and tumor necrosis factor- from granulocytes following exposure to respiratory viral particles, and the effects of exposure to sulfur dioxide and sulfite aerosols on neutrophil function (Kricka, 1995).

Luminol is currently used by most police agencies in the U.S. as a forensic tool for the detection of trace blood patterns at crime scenes; it is applied as an aerosol in a mixture with sodium perborate, sodium carbonate, and distilled water (Kricka, 1995; Yeshion, 1996).

In clinical settings, luminol has been used for the treatment of the patches of baldness caused by the autoimmune disease alopecia (Irie, 1960a), for the treatment of fluid accumulation in tissues of chronically ill patients (Irie, 1960b), and for the promotion of blood clotting (Irie, 1960c) and wound healing (Irie, 1961). There is no evidence, however, that it is currently used as a therapeutic agent. Luminol has never been approved for marketing by the FDA (Diogenes, 1997).

6.0 ENVIRONMENTAL OCCURRENCE

No data were found.

7.0 HUMAN EXPOSURE

Law enforcement workers may be exposed to luminol during its use as a forensic tool for the detection of trace blood patterns at crime scenes (Kricka, 1995; Yeshion, 1996). Other workers may be exposed to luminol and its metabolite 3-aminophthalic acid while using it to conduct biochemical assays. No data were available on the number of workers exposed to luminol.

Although luminol has been used in the past in limited clinical trials (see **Section 5.0**), no data indicate any past or current use of luminol as a registered therapeutic agent.

8.0 REGULATORY STATUS

No data were found.

9.0 TOXICOLOGICAL DATA

Summary: No adverse or toxic side effects were observed in limited clinical trials of luminol conducted in the 1960s.

In vitro, the chemiluminescence-producing oxidation of luminol by the enzyme horseradish peroxidase yields three metabolites, one of which is 3-aminophthalic acid. The other two metabolites were not identified.

The oral LD₅₀ for luminol in rats was >500 mg/kg (>2.82 mmol/kg). Increased excretion of urine (diuresis) and sodium (natriuresis), and decreased arterial blood pressure were observed in female dogs following intravenous (i.v.) injection of a single dose of 2.5 mg (0.014 mmol) luminol (duration of observation period was not specified). No adverse effects were observed in mice injected intraperitoneally (i.p.) with a single dose of 1 to 5 mg (0.006 to 0.03 mmol) luminol and observed for 4 weeks.

Luminol was negative *in vitro* for the induction of gene mutations in *Salmonella typhimurium*, with and without metabolic activation, and in *Escherichia coli*, without metabolic activation. *In vitro*, in Chinese hamster V79 cells, luminol, at doses of 250, 500, and 1000 µM, greatly enhanced the frequency of SCE but only when treatment occurred during S-phase in the presence of bromodeoxyuridine. Luminol inhibited repair of DNA damage induced by methyl methanesulfonate (MMS) in Chinese hamster ovary cells, but had no apparent effect on UV-induced strand breaks. Luminol was reported to increase the efficiency of intrachromosomal homologous recombination in Chinese hamster A238 cells, and to affect the rate of single DNA exchanges and gene conversion (double exchanges) in LMtk⁻ and HeLa cells, respectively, transformed with plasmid DNAs which contain copies of the neo-gene with non-overlapping deletions.

Luminol was reported to inhibit poly(ADP-ribose) polymerase, with greater efficiency than 3-aminobenzamide. Similar to other inhibitors, treatment of oncogene-transformed NIH-3T3 cells with luminol (250, 1000 µM) for 12 days after plating resulted in the marked appearance of flat cells, possibly by eliminating exogenous transforming genes, irrespective of the properties of the transforming gene products. Similarly, luminol (at 1000 µM) suppressed G₁ arrest and enhanced G₂ arrest in mouse embryonic fibroblast C3D2F1 3T3-a cells irradiated with 2 Gy gamma radiation. Luminol, at 200 to 400 µM, also inhibited slow and fast potentially lethal damage (PLD) repair in V79 cells irradiated with 11 Gy x-rays

In rats, luminol (2 or 6%/kg feed; 110 or 340 mmol/kg feed) administered for 10 weeks starting 2 weeks after a single intraperitoneal (i.p.) injection of 200 mg/kg *N*-nitrosodiethylamine (DEN) did not affect the average liver weight or the development of liver foci. However, luminol at concentrations of 3 or 6%/kg feed (170 or 340 mmol/kg feed) administered concurrently with 0.05% (2 mmol) phenobarbital in the diet for 10 weeks following injection of 200 mg/kg DEN inhibited phenobarbital-dependent liver enlargement and development of glutathione *S*-transferase placental (GST-P)-positive liver foci. Luminol exerted no effect at the 1% or 2% level (56 or 110 mmol/kg feed).

9.1 General Toxicology

9.1.1 Human Data

No adverse or toxic side effects were observed in the clinical trials conducted by Irie (1960a, b, c; 1961) and briefly described in **Section 5.0**. No other human toxicological data were found.

9.1.2 Chemiluminescence

The reaction of luminol with oxygen species generated by cells produces an excited intermediate that emits light (chemiluminescence) as it relaxes to a stable state (for reviews see Briheim et al., 1984; Kahl et al., 1987; Radi et al., 1993; Lundqvist and Dahlgren, 1996). Luminol chemiluminescence occurs in aqueous solution with hydrogen peroxide and a supplemental oxidant such as ferricyanide, hypochlorite, persulfate, or the hydroxyl radical generated from hydrogen peroxide, and a metal derivative such as hemin. It also occurs in dipolar aprotic solvents such as dimethylsulfoxide in the presence of oxygen and a strong base (Rauhut, 1985). Results from some studies indicate that luminol chemiluminescence in *in vitro* mammalian systems requires the presence of the enzyme myeloperoxidase (Dahlgren and Stendahl, 1983) and Fe^{2+} (Klinger et al., 1996) to proceed, and is greatly enhanced in the presence of bicarbonate (Puget and Michelson, 1976; Radi et al., 1993). Luminol-dependent chemiluminescence has been observed during the respiratory burst of macrophages and neutrophils (Allen, 1986; cited by Radi et al., 1993; Lundqvist et al., 1995). The precise nature of the oxidizing species depends on the cell typ. (Aitken et al., 1992).

9.1.3 Metabolism

In vitro, the chemiluminescence-producing oxidation of luminol by the enzyme horseradish peroxidase yields three metabolites, one of which is 3-aminophthalic acid (Jansen and

Van den Berg, 1991). The other two metabolites were not identified.

Results from a study conducted by Buturlakin et al. (1975) indicate that luminol binds to human serum albumin *in vitro*. Addition of human serum albumin to a 3 mM solution of luminol increased the intensity of the luminescence as a function of albumin concentration.

9.1.4 Acute Exposures

The only available LD₅₀ data for luminol are presented in **Table 1**; other acute exposure data are presented in **Table 2**.

Table 1. LD₅₀ Values for Luminol

Route	Species (strain)	LD ₅₀	Reference
oral	rat (strain not provided)	>500 mg/kg (>2.82 mmol/kg)	Natl. Acad. Sci. (1953; cited by RTECS, 1995)

9.1.4.1 Intravenous Injection

Increased excretion of urine (diuresis) and sodium (natriuresis), and decreased arterial blood pressure were observed in female dogs (strain not provided) following i.v. injection of a single dose of 2.5 mg (0.014 mmol) luminol (duration of observation period was not specified) (Irie and Mendlowitz, 1970).

9.1.4.2 Intraperitoneal Injection

No adverse effects were observed in mice (strain not provided) injected i.p. once with luminol at 1.5, 2, 2.5, 3, 3.5, 4, 4.5, or 5 mg (0.006, 0.008, 0.011, 0.014, 0.017, 0.020, 0.023, 0.025, 0.028 mmol) and observed for 4 weeks (Irie, 1960a).

Table 2. Acute Toxicity of Luminol

Species, Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/Observation Period	Results/Comments	Reference
9.1.4.1 Intravenous Injection						
dog (strain and age n.p.)	exposed: 5 F controls: each dog served as its own control	luminol, purity n.p.	2.5 mg (0.014 mmol) administered i.v. (vehicle n.p.)	single dose; duration of observation period n.p.	Increased excretion of urine (diuresis), increased excretion of sodium (natriuresis), and decreased arterial blood pressure were observed following injection of luminol.	Irie and Mendlowitz (1970)
9.1.4.2 Intraperitoneal Injection						
mouse (strain and age n.p.)	exposed: 5 mice per dose (sex n.p.) controls: 0	luminol, purity n.p.	1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, or 5 mg (0.006, 0.008, 0.011, 0.014, 0.017, 0.020, 0.023, 0.025, 0.028 mmol) administered i.p. (vehicle n.p.)	single dose; mice were observed for 4 wk	No adverse effects were observed.	Irie (1960a)

Abbreviations: F = female; i.p. = intraperitoneal; i.v. = intravenously; n.p. = not provided

9.1.5 Short-Term and Subchronic Exposures

No data were found.

9.1.6 Chronic Exposures

No data were found.

9.2 Reproduction and Development

No data were found.

9.3 Carcinogenicity

No data were found.

9.4 Genotoxicity

The studies described in this section are presented in **Table 3**.

9.4.1 Prokaryotic Systems

As reported by Zeiger et al. (1992), luminol did not induce *his* gene mutations in *Salmonella typhimurium*. Strains TA97, TA98, TA100, TA1535, and TA1537 were exposed to doses ranging from 1000 to 10,000 µg/plate (5.64 to 56.45 µmol/plate) using the pre-incubation method in either the presence or absence of 10% or 30% rat or hamster liver metabolic activation.

Luminol, in the absence of metabolic activation, was also reported as negative for the reversion of *Escherichia coli* to streptomycin independence (Szybalski, 1958). A paper disk method was used; no other details were provided.

9.4.2 *In Vitro* Mammalian DNA Damage

Luminol, at doses of 250, 500, and 1000 µM, greatly enhanced the frequency of SCE in

Chinese hamster V79 cells when treatment occurred during the S-phase in either the first or the second cell cycle in the presence of bromodeoxyuridine (Ikushima, 1990). Luminol was ineffective in inducing SCE when treatment occurred during the G₁ phase of the cell cycle. The mechanism was thought to be related to the ability of luminol to inhibit poly(ADP-ribose) synthetase. The author noted that, on a molar basis, luminol was more potent in inducing SCE than 3-aminobenzamide, a well-known inhibitor of poly(ADP-ribosyl)ation.

Table 3. Genotoxicity of Luminol

Test System	Biological Endpoint	S9 Metabolic Activation	Chemical Form, Purity	Dose	Endpoint Response	Comments	Reference
9.4.1 Prokaryotic Systems							
<i>Salmonella typhimurium</i> strains TA100, TA97, TA98, TA1535, TA1537	<i>his</i> gene mutations	-/+ S9 10% and 30%, rat and hamster	luminol, 97%	100 to 10,000 µg/plate (5.64- 56.45 µmol/plate)	negative/negative	The pre-incubation method was used.	Zeiger et al. (1987)
<i>Escherichia coli</i>	reversion to streptomycin independence	-	luminol, n.p.	n.p.	negative	The paper disk method was used	Szybalski (1958)
9.5.2 In Vitro Mammalian DNA Damage							
Chinese hamster V79 cells	sister chromatid exchanges (SCE)	-	luminol, n.p.	250, 500, or 1000 µM	positive	SCE frequency greatly enhanced when treatment occurred during the S-phase in either the first or the second cell cycle in the presence of bromodeoxyuridine. Ineffective in inducing SCE when treatment occurred during G ₁ . Mechanism thought to be related to inhibition of poly(ADP-ribosylation). Author noted that, on a molar basis, luminol was more potent than 3-aminobenzamide, an inhibitor of poly(ADP-ribosylation), in inducing SCE.	Ikushima (1990)
n.p.	intrachromosomal homologous recombination	-	luminol, n.p.	n.p.	positive		Abramian et al., (1994 abstr.)
Chinese hamster ovary (CHO-K1) cells	inhibitory effects on repair of UV or MMS induced DNA damage, analyzed by alkaline elution and alkaline sucrose sedimentation.	-	luminol, n.p.	1000 or 2000 µM	positive for inhibition of DNA damage induced by MMS; negative for inhibition of UV induced strand breaks	Data on luminol by itself n.p.	Lee-Chen et al., 1994.

TOXICOLOGICAL SUMMARY FOR LUMINOL [521-31-3]

07/97

LMtk ⁻ and HeLa cells	LMtk ⁻ cells: single DNA exchanges HeLa cells: gene conversion (double exchanges)	-	luminol, n.p.	n.p.	positive	Cells transfected with plasmid DNA which contained copies of the neo-gene with non-overlapping deletions. No data provided.	Glebov et al. (1994 abstr.)
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Abbreviations: n.p. = not provided

Post-treatment with 1000 or 2000 μM luminol had no apparent effect on the repair of UV-induced DNA strand breaks in CHO-K1 cells when analyzed by alkaline elution and alkaline sucrose sedimentation (Lee-Chen et al., 1994). Luminol did, however, inhibit the repair of damage induced by methyl methanesulfonate (MMS). No data were given on the DNA-damaging effects of luminol by itself.

Luminol was reported to increase the efficiency of intrachromosomal homologous recombination in Chinese hamster A238 cells (Abramian et al., 1994 abstr.), and to affect the rate of single DNA exchanges and gene conversion (double exchanges) in LMtk⁻ and HeLa cells, respectively, transformed with plasmid DNA which contained copies of the neo-gene with non-overlapping deletions (Glebov et al., 1994 abstr.).

9.5 Other Toxic Effects

9.5.1 Effects on Enzyme Activity

Luminol inhibits poly(ADP-ribose) polymerase activity, and consistent with the effects of other inhibitors, treatment of oncogene-transformed NIH-3T3 cells with luminol (250, 1000 μM) for 12 days after plating resulted in the marked appearance of flat cells (Nagao et al., 1990; 1991). The investigators concluded that luminol [and other poly(ADP-ribose) polymerase inhibitors] eliminated exogenous transforming genes, irrespective of the properties of the transforming gene products. Also consistent with other poly(ADP-ribose) polymerase inhibitors, luminol (at 1000 μM) suppressed G₁ arrest and enhanced G₂ arrest in mouse embryonic fibroblasts C3D2F1 3T3-a cells irradiated with 2 Gy gamma radiation (Nozaki et al., 1994), while at 200 to 400 μM it inhibited slow and fast potentially lethal damage (PLD) repair in V79 cells irradiated with 11 Gy x-rays (Utsumi et al., 1994). In the latter study, luminol was

reported to be 10 times more effective than 3-aminobenzamide.

9.5.2 Promotion of Liver Foci

In male Fischer 344 rats, administration of luminol at concentrations of 2 or 6%/kg feed (110 or 340 mmol/kg feed) for 10 weeks, starting 2 weeks after a single i.p. injection of 200 mg/kg *N*-nitrosodiethylamine (DEN), had no clear effect on the average liver weight and had no effect on the development of liver foci (Tsujiuchi et al., 1990). Concurrent administration of luminol at concentrations of 3 or 6%/kg feed (170 or 340 mmol/kg feed) with 0.05% (2 mmol) phenobarbital in the diet for 10 weeks following injection of 200 mg/kg DEN inhibited phenobarbital-dependent liver enlargement and development of glutathione *S*-transferase placental (GST-P)-positive liver foci observed in rats fed PB alone. Luminol exerted no effect at the 1% or 2% level (56 or 110 mmol/kg feed). All rats were killed immediately after the end of treatment (12 wk after injection of DEN).

10.0 STRUCTURE-ACTIVITY RELATIONSHIPS

A number of 2,3-dihydrophthalazine-1,4-dione derivatives possess anti-neoplastic activity *in vitro* (Hall et al., 1992). Of 28 derivatives tested (luminol was not included), most demonstrated potent cytotoxicity towards murine leukemia and human tumor cell lines. Only some of the tested derivatives, however, were active against *in vitro* growth of bronchogenic lung, osteosarcoma, and glioma cell lines.

11.0 ONLINE DATABASES AND SECONDARY REFERENCES

11.1 Online Databases

Chemical Information System Files

ISHOW (Information System for Hazardous Organics in Water)

SANSS (Structure and Nomenclature Search System)

TSCAPP (Toxic Substances Control Act Plant and Production)

DIALOG Files

359 Chemical Economics Handbook

158 DIOGENES FDA Regulatory Updates

Internet Databases

Code of Federal Regulations full text. 1996 versions of various titles via GPO Gate, a gateway by the Libraries of the University of California to the GPO Access service of the Government Printing Office, Washington, DC. Internet URL <http://www.gpo.ucop.edu/>

National Library of Medicine Databases

EMIC and EMICBACK (Environmental Mutagen Information Center)

STN International Files

BIOSIS (Biological Abstracts)

CA File (Chemical Abstracts)

CANCERLIT

CEN (Chemical & Engineering News)

CIN (Chemical Industry Notes)

CSNB (Chemical Safety News Base)

EMBASE (Excerpta Medica)

HSDB (Hazardous Substances Data Bank)

MEDLINE (Index Medicus)

PROMT (Predicasts Overview of Markets and Technology)

Registry File

RTECS (Registry of Toxic Effects of Chemical Substances)

TOXLINE

TOXLIT

TOXLINE includes the following subfiles:

Toxicity Bibliography	TOXBIB
International Labor Office	CIS
Hazardous Materials Technical Center	HMTC
Environmental Mutagen Information Center File	EMIC
Environmental Teratology Information Center File (continued after 1989 by DART)	ETIC
Toxicology Document and Data Depository	NTIS
Toxicology Research Projects	CRISP
NIOSHTIC7	NIOSH
Pesticides Abstracts	PESTAB
Poisonous Plants Bibliography	PPBIB
Aneuploidy	ANEUPL
Epidemiology Information System	EPIDEM
Toxic Substances Control Act Test Submissions	TSCATS
Toxicological Aspects of Environmental Health	BIOSIS
International Pharmaceutical Abstracts	IPA
Federal Research in Progress	FEDRIP
Developmental and Reproductive Toxicology	DART

11.2 Secondary References

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