



Bromodeoxyuridine

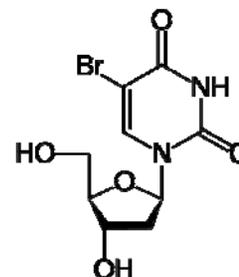
Introduction

Synonyms: Uridine, 5-bromo-2'-deoxy-; 5-BRDU; 5-Bromodeoxyuridine; 5-Bromo-2'-deoxyuridine; 2'-Deoxy-5-bromouridine; 5-Bromo-2'-desoxyuridine; 5-Bromodesoxyuridine; 5-Bromouracil deoxyriboside; 5-Bromouracil-2-deoxyriboside; Bromodeoxyuridine; Broxuridin; broxuridina; Broxuridine; 5-BDU; BRUDR; BUdR; NSC 38297.

CAS Number: 59-14-3

Formula: C₉H₁₁BrN₂O₅

Molecular Weight: 307.11 g/mole



Bromodeoxyuridine (BrDU) is a synthetic nucleoside that is an analogue of thymidine. BrDU is commonly used in the detection of proliferating cells in living tissues. BrDU can be incorporated into the newly synthesized DNA of replicating cells (during the S Phase of the cell cycle), substituting for thymidine during DNA replication.

Antibodies specific for BrDU can then be used to detect the incorporated chemical thus indicating cells that were actively replicating their DNA. Binding of the antibody requires denaturation of the DNA, usually by exposing the cells to acid or heat. Because BrDU can replace thymidine during DNA replication, it can cause mutations, and its use is therefore potentially a health hazard.

At room temperature, it exists as a white crystalline powder. BrDU is characterized as a weak mutagenic agent and may be harmful if ingested, inhaled or in contact with bare skin. The primary harmful effects are genetic mutation, anemia, reproductive disorders (fetal death or abnormality), cataracts, and skin irritation. The dose to induce death is high (0.9 kg drug per kg body weight orally in mice). It has low toxic and carcinogenic potential.

Because BrDU has cytotoxic, teratogenic, and mutagenic properties, exposure presents potential health and safety hazards to laboratory staff, animal handlers and other personnel who may be accidentally exposed to BrDU.

As a reproductive toxin BrDU would be considered a “particularly hazardous substance” under the OSHA lab standard (29 CFR 1910.1450) which requires use in a closed system or containment such as a fume hood or ventilated enclosure, a designated area for its use with appropriate signage, provisions for clean up and decontamination, and provisions for waste removal.

Potential Hazards

Employees may be exposed to BrDU in the bedding, dust, cages and excretions of rodents or other animals given the drug. Risks are negligible, however, given the low dose of the agent typically used in animals and the fact that virtually all of the drug should bind to cellular nucleic acids in the recipient animal or be metabolized.



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According to the Hazardous Substances Data Bank (HSDB) BrdU is degraded at a fairly rapid rate in mice and rats upon injection, in at least two metabolic pathways; one is hydrolysis at the glycosyl bond to yield bromouracil and 2-deoxyribose which is presumably then further metabolized. The other is debromination which is evidenced by liberation of bromide ion. The further fate of the remainder of the molecule has not been investigated.

Note: Because BrDU has potential teratogenic and mutagenic properties, pregnant women should consult with their physician and avoid handling BrDU or use caution while handling the chemical or potentially contaminated bedding and animals.

Personal Protection

All personnel should wear appropriate Personal protective Equipment (PPE). The appropriate PPE consists of:

- Examination gloves.
- Safety glasses or safety goggles (ANSI Z-87 approved).
- Lab coat.
- Appropriate laboratory attire.
- Half face respirator when aerosol exposure hazard exists (or if not handled in a containment, i.e. fume hood or ventilated dump station).

Procedures

Animals receiving BrDU must be housed in an animal room designated for use of carcinogens and reproductive toxins with the appropriate sign.

Animal bedding should be made of corn husks (Bed-o-Cobs is commonly used for rodents), or other similar material to minimize dust generation.

Cardboard, paper or other friable materials should be avoided whenever possible. A plastic liner which can simply be rolled up and disposed of should be placed under the bedding when cage changes won't take place in a cage change cabinet.

Animals can be manipulated outside of a fume hood while using the appropriate PPE.

1) Acute administration

Acute administration is typically conducted by injecting a specified dose of BrDU IV or IP into the animal subject a few hours before euthanasia.

Used needles must be disposed of in an approved sharps container immediately after use. Used needles should not be set on the bench, sheared, bent or re-capped prior to disposal.

Whenever feasible, self-sheathing needles should be used to avoid the potential for accidental needle stick injuries.

To avoid the potential for inhalation of aerosols, the injection of BrDU into research animals should always be conducted in a certified Class II or III biosafety cabinet.



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2) Chronic Administration

BrDU may be administered to animals via IV or IP injection, supplied in the drinking water or via an osmotic pump.

Chronic administration of BrDU via IV or IP should follow the same injection procedures as acute administration above.

Mice may be given BrDU in the drinking water (0.25-1 mg/ml) daily for up to 6 weeks or as daily i.p. injections (~2 mg in 100µl of sterile saline) for up to 1 week. BrDU-containing water bottles are shielded from light to prevent BrDU degradation and the water is replaced twice per week. 1% glucose may be included in the drinking water during the first week to overcome taste aversion. Total duration of the procedure is 1 hr to 6 weeks, after which animals are euthanized. Drinking water solutions of BrDU must be prepared in an appropriate chemical fume hood. Waste drinking water should be diluted to a 10% final solution of fresh mercury-free bleach, and may then be disposed in the drain.

Water bottles should be washed with a fresh 10% bleach solution.

Osmotic pumps should be prepared in an appropriate chemical fume hood. Pumps should only be handled with gloved hands. Appropriate PPE should be worn.

Waste Disposal and Labeling

Concentrated bromodeoxyuridine must be disposed of as a hazardous chemical waste and disposed of by EHS. If the waste is in a very dilute concentration (i.e. <1%) it can be disposed to the sanitary sewer with copious amounts of additional water during disposal.

In this state, it is acceptable to dispose of potentially metabolized BrDU contaminated animal bedding as non-hazardous solid waste.

- The animal bedding must be changed or emptied into a bag under a fume hood or a ventilated dump station.
- Wear all appropriate Personal Protective Equipment (PPE) during handling.
- Bags should be closed and secured with a wire tie or tape before removing from the ventilated dump station or fume hood.
- Contaminated PPE should be bagged and placed in the facility dumpster for disposal.
- Bags may be labeled "BrDU" and "Non-Hazardous Waste" and placed in the facility dumpster.

All animal carcasses should be packaged, labeled, frozen, and collected for disposal as medical waste. See Biohazardous Waste Disposal Policy at:

http://www.ehs.indiana.edu/bio_waste.shtml.

Chemical Spills

1) Major spills of stock solutions

- Isolate area and report spill to Environmental Health and Safety: (812) 855-6311.
- Direct contact with the stock solution should be avoided.



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2) Minor spills

- Contain spill and clean up bulk material using paper towel or absorbent pads from nearest chemical spill kit.
- For spills of powder, it may be helpful to wet the absorbent material. Wash the area with a 10% fresh bleach solution and then soap and water.
- In addition to the required PPE an additional layer of Nitrile gloves or equivalent should be used whenever spills are handled.

References

Bromodeoxyuridine, Material Safety Data Sheet, Product No B9285, Sigma-Aldrich Chemical Company.

Hazardous Substances Data Bank (HSDB), Bromodeoxyuridine, Metabolism/Metabolites. Kriss JP, Revesz L; Cancer Res 22: 254-65 (1962) as cited in NIH Division of Occupational Health and Safety; Safety Data Sheet for 5-Bromo-2'-deoxyuridine.

Sax, N.I., Dangerous Properties of Industrial Materials, 6th Ed., Van Nostrand Reinhold, New York. 1984. p. 525.