THE INTELLIGENT CHEMICAL

ISOPROTHIOLANE

NIHON NOHYAKU CO., LTD.
**Chemical and Physical Properties**

- **Common name:** Isoprothiolane
- **Chemical name (IUPAC):** disopropyl 1,3-dithiolan-2-ylidenemalonate
- **Trade name:** Fuji-One
- **Melting point:** 54.6-55.2°C
- **Vapor pressure:** $4.93 \times 10^{-4}$ Pa (25°C)
- **Solubility:** water; 48.5mg/L acetone; 4,061g/L chloroform; 4,126g/L
- **Partition coefficient:** log Pow = 2.80

**Structure formula**

![Structure formula of Isoprothiolane]

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**Toxicology (technical)**

**Acute toxicity**

- Oral: Rat LD$_{50}$(mg/kg) $\geq 300 < $LD$_{50} \leq 2,000$
- Dermal: Rat LD$_{50}$(mg/kg) $\geq 2,000$
- Inhalation: Rat LC$_{50}$(mg/L/4h) $\geq 2.77$
- Skin Irritation: Guinea pig Moderate irritant
- Eye irritation: Rabbit Slightly irritant
- Skin sensitization: Guinea pig Positive

**Acute toxicity to aquatic organisms**

- Carp LC$_{50}$ (96h): 11.4 mg/L
- Daphnia EC$_{50}$ (48h): 19.0 mg/L
- Algae ErC$_{50}$ (0-72h): 10.8 mg/L

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**Characteristics of Isoprothiolane**

1. Both preventive and curative effect on rice blast
2. Effective on every stage of life cycle of blast fungus
   (Strong inhibition on penetration stage)
3. High efficacy against leaf and panicle blast
4. Long lasting effect and strong systemic action
5. Additional effect on rice growth as a PGR and suppression of Brown Plant Hopper (BPH), which are registered in Japan

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**Mode of Action**

**F: Lipid Synthesis and Membrane Integrity**

- **F2:** phospholipid biosynthesis $\rightarrow$ methyltransferase
  - #6 phosphorothiolates & dithiolanes
  - phosphorothiolates
    - pyrazophos
    - iprobenfos
    - edifenfos
  - dithiolanes
    - Isoprothiolane

- **F3:** lipid peroxidation (prop.)
  - #14 aromatic hydrocarbons & heteroaromatics
  - aromatic hydrocarbons
    - tecnazene (TCNB)
    - dicyan
    - quintozone (PCNB)
    - tolclofos-methyl
    - bipheny
    - chloroneb
  - 1,2,4-thiadiazole
    - etridiazole

- **F4:** cell membrane permeability, fatty acids (prop.)
  - #28 carbamates
    - propamocarb
    - iodocarb
    - prothiocarb

- **F6:** microbial disrupters of pathogen cell membranes
  - #44 Microbial (Bacillus sp.)
  - Bacillus sp. and the fungicidal lipopeptides produced

- **F7:** cell membrane disruption (prop.)
  - #46 plant extracts
    - Melaleuca alternifolia (Tea Tree Extract)

- Isoprothiolane belongs to F2 class (code6) fungicides in FRAC MOA classification and affects lipid metabolism and/or bio-synthesis of fatty acid such as methylation of phospholipid.
- No resistant isolate is observed to Isoprothiolane as written in p. 4.
- This figure is referring to FRAC information (www.frac.info).
Inhibitory effect of Isoprothiolane on the infection cycle of rice blast (EC$_{90}$)

- IPT affects every stage of infection cycle of rice blast
- Penetration stage is most sensitive → Main Target

**Action of Isoprothiolane against blast fungi-1 Appressorium formation**

Method:
The appressorium formed in the absence (UTC) or presence of IPT was removed from plant cell and supporting surface of appressorium was observed by electron microscope.

Results
In UTC hollow as the trace of penetration hyphae was observed. In IPT treated no hollow or trace was observed.

**Action of Isoprothiolane against blast fungi-2 Hyphae growth**

IPT treatment
↓ Thin cell wall
↓ Short cell
↓ Hyphae with abnormal shape is formed
↓ Normal growth of hyphae is inhibited
Biological activity of Isoprothiolane to rice leaf blast (Pot trials)

**Test 1: Curative**

- **Year:** 2013
- **Location:** NNC Research center
- **Treatment:** 1 day after inoculation
- **Assessment:** 7 days after treatment

- IPT has an excellent efficacy on rice blast
- Both the preventive and curative efficacy were confirmed

**Test 2: Preventive and Curative**

- **Year:** 2016
- **Location:** NNC Research center
- **Preventive:** Treated before inoculation on the same day
- **Curative:** Treated on 1 day after inoculation

- IPT 400 ppm
- 200 ppm
- 80 ppm

**Preventive**

**Curative**

IPT: Isoprothiolane

Biological activity of Isoprothiolane to rice blast (Field trials)

**Panicle blast: Curative (Japan)**

- **Year:** 2016
- **Location:** Japan
- **Treatment:** 1 time at 24th August, at heading stage, curative condition
- **Assessment:** 18th September

- IPT 400 ppm
- Tricyclazole 417 ppm
- Azoxystrobin 80 ppm

**Leaf & Panicle blast: Preventive (Malaysia)**

- **Year:** 2010
- **Location:** Malaysia
- **Treatment:** 17th & 24th July for Leaf blast, 25th Aug. & 2nd Sep. for Panicle blast
- **Assessment:** 9th Aug. & 15th Sep.

- IPT 400 gai/ha
- Trifloxystrobin+tebuconazole 25+50 % 120 gai/ha
- Difenoconazole 25 % 50 gai/ha
- Azoxystrobin 22.94 % 57.33 gai/ha

IPT has better curative efficacy than competitors and similar preventive efficacy to competitors even in the field.
Sensitivity test of Isoprothiolane against blast fungus in Japan

- No sensitivity shift is observed more than 30 years since IPT was launched in Japan (1975).
- Resistance risk of IPT against rice blast is quite low.
- No cross resistance is observed between IPT and other F2 class fungicides of FRAC (data not shown).

Best Spray Timing for Leaf Blast

- Normal: 1 time
- Additional (Emergency): Immediately when you find lesions

Best Spray Timing for Panicle Blast

- Normal: 2 times
- Booting 50% Heading Full Heading Ripening

Translocation of Isoprothiolane between leaves

Method: 400 ppm of $^{14}$C-labeled IPT was applied to the 3rd leaf blade of 4-leaf stage seedling. Translocation of IPT was examined by autoradiography.

High translocation activity was observed in rice seedling by autoradiography. Systemic action is expected from leaves to whole plants.
**PGR effect including the efficacy to rice blast - Yield Increase**

Location: Vietnam in 2017  
Rice variety: Sticky rice  
Treatment: 2 times (before heading and full heading stage)

High yield was shown by the treatment with Isoprothiolane

**PGR/Rice Improvements - Effects of Isoprothiolane**

- Inhibit aging  
  Benzyladenine (hormone)
- Suppress spindly growth  
  Ethylene (hormone)
- Elongate roots  
  IAA (hormone)
- Improve photosynthesis  
  Chlorophyll
- Enhance uptake of nutrients & water  
  Acid phosphatase (enzyme)
- Elongate roots
- Improve photosynthesis
- Inhibit aging
- Prevention of aging
- Cell extension, improvement of root growth
- Prevention of chlorophyll degradation
- Increase in ability of respiration and amount of transpiration
- Maintain leaf color, suppression of wither of lower leaves

**PGR/Mechanism of yield increase by the improvement of grain ripening Isoprothiolane**

- Increase of endogenous IAA
- Inhibition of lignin synthesis
- Prevention of aging
- Improve in ability of respiration and amount of transpiration
- Improvement in the ability of photosynthesis
- Improvement of grain ripening
- Yield increase

IAA: Indole Acetic Acid  
IPT: Isoprothiolane  
UTC: Untreated Control

PGR/Improvement of grain ripening- Translocation of nutrients

Isoprothiolane

Treatment: Isoprothiolane 12% Granule 4,800 kg/ha

Chase and assessment of translocation of carbohydrate using radioisotope ($^{14}$CO$_2$)

Panicle was apparently darker color since 4 days after treatment

It means higher ability of photosynthesis and much starch accumulation in panicle.

Improvement of grain ripening- Inferior grains

Superior grains (non-colored)

Grains of 1st panicle branch and top grain of 2nd panicle branch

Inferior grains (red-colored)

Grains except top one in 2nd panicle branch

Isoprothiolane improves grain ripening of inferior grains

PGR/Improvement of grain ripening- Inferior panicle

Assessment of all panicle

Grain ripening ratio (%)

100
90
80
70
60
50
40
30
20
10
0

IPT 40EC 400 ppm
UTC

+ 6.2%

Assessment of inferior panicle

1st panicle branch
2nd panicle branch

Bootimg Full-heading
IPT 40 EC / 400 ppm
UTC

+ 18.5%

+ 8.4%

Location: Saitama Pref., Japan (2014)
Cultivar: Ayanokagayaki
Treatment: 19th Aug. (11 days before heading)

Location: Fukushima Pref., Japan (1992)
Cultivar: Hitomebore
Treatment: 14th (Booting)& 24th (Full-heading) Aug.
Inferior panicle: the third shortest stem in a hill

Isoprothiolane improves grain ripening of inferior panicle and inferior grains
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