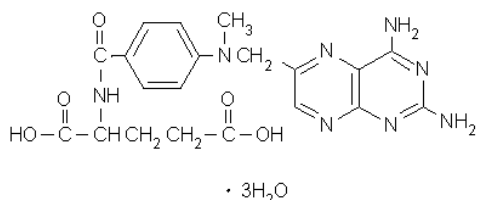


## 06563 Methotrexate

(4-Amino-10-methylfolic acid, (+)-Amethopterin, Methylaminopterine, 4-Amino-N<sup>10</sup>-methylpteroyl-L-glutamic acid, Antifolan, MTX)

**CAS number:** 59-05-2

Appearance:	Yellow powder <sup>3</sup>
Molecular formula:	C <sub>20</sub> H <sub>22</sub> N <sub>8</sub> O <sub>5</sub>
Molecular weight:	454.44 g/mol
Mp:	185-204 °C (dec.) <sup>2</sup>
[α] <sub>D</sub> <sup>20</sup> :	+19 ± 3° (c = 2 in NaOH 0.1M) <sup>3</sup>
[α] <sub>546</sub> <sup>20</sup> :	+24 ± 3° (c = 2 in NaOH 0.1M) <sup>3</sup>
pKa1:	3.8 (temperature not specified). <sup>4</sup>
pKa2:	4.8 (temperature not specified). <sup>4</sup>
pKa3:	5.6 (temperature not specified). <sup>4</sup>
Absorbance:	In 0.1 N HCl: λ <sub>max</sub> = 244 nm, 307 nm <sup>2,5</sup>
ε (257nm):	22.3 (0.1 N NaOH) <sup>2</sup>
ε (302nm):	22.7 (0.1 N NaOH) <sup>2</sup>
ε (370nm):	7.3 (0.1 N NaOH) <sup>2</sup>



Storage Temperature -20 °C. Protection from light for long-term storage has been suggested.<sup>4</sup>

### Applications:

MTX, an anticancer drug, is structurally similar to folic acid. MTX (Amethopterin) and aminopterin are both potent, stoichiometric inhibitors of dihydrofolate reductase (DHFR). (Dihydrofolate reductase is an enzyme involved in cellular DNA synthesis.) MTX appears to be preferred to aminopterin (which is photosensitive and toxic). The stability and low toxicity of MTX also favor its use in the selection of hybridomas.<sup>7</sup> The metabolism and pharmacokinetics of MTX have been studied.<sup>8-10</sup> The reaction between MTX and dihydrofolate reductases has been described, and a three-dimensional structure of the complex has been published.<sup>11,12</sup> Resistance to the drug as a result of permeability changes has been studied.<sup>13</sup>

### Preparation Instructions:

MTX was reported insoluble in water, ethanol, chloroform and ether. It is, however, soluble in solutions of mineral acids and in dilute solutions of alkali hydroxides and carbonates.<sup>4</sup> Compound routinely assayed at 20 mg/mL in NaOH 0.1M.



For cell culture work, a stock solution of the compound methotrexate is prepared using a minimum amount of 1 M NaOH and then diluted with saline or medium. The diluted stock is stable at 4-8 °C for about a week, or at -20 °C for about a month.<sup>6</sup>

## References

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