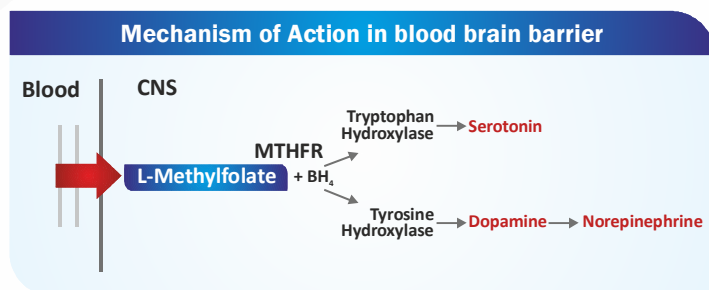


Folate deficiency has also been linked to courses of depressions that are more severe, longer in duration, and treatment resistant. A deficiency may result in inadequate CNS synthesis of serotonin, norepinephrine, and dopamine.



**L- Methylfolate developed by Puneet Laboratories is the optically bioactive L-form having specific optical rotation between +34° to +42°**

Due to its unique ability to provide the complete nutritional benefit of folate supplementation, LMF provides an effective folate supplementation in the following conditions:

- Fertility support
- Prenatal care
- Cardiovascular diseases
- Diabetic neuropathy
- Dementia
- Depressive disorders

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\* L-Methylfolate



**The Mark of Innovative Chemistry!**

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# L-METHYLFOLATE

## Optically Bioactive form of Folate



## L-Methylfolate (LMF) - Optically Bioactive form of Folate

LMF is highly bioavailable source of folic acid. It is the natural, active form of folic acid which is an integral component of prenatal care, homocysteine management, depression treatment, dementia and cardiovascular concerns. LMF is a vitamin essential for reproductive health.

## Importance of folate and its deficiency

Folate is a water soluble B vitamin (B9), one of the 13 essential vitamins required for several important biological processes, which include

- Normal cell growth and replication
- Nucleic acid synthesis
- Red blood cell maturation
- DNA repair
- Modulation of the amino acid homocysteine
- Brain development

## Folic acid and LMF

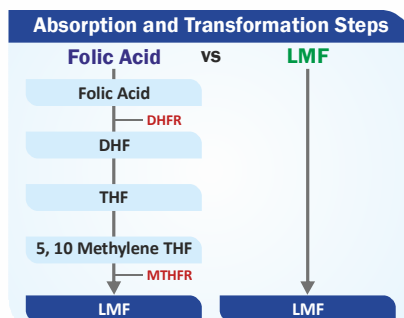
Regular folic acid undergoes a 4-step enzymatic conversion process to achieve LMF - the active form of folic acid used by the body. Dihydrofolate Reductase (DHFR) converts folic acid to dihydrofolate (DHF), DHF is then converted to tetrahydrofolate (THF), THF is converted to 5,10-methylene THF, and the last conversion step involves an enzyme Methylene tetrahydrofolate Reductase (MTHFR) converting 5,10-methylene THF to LMF.<sup>1</sup>

However research has shown that the conversion of folic acid into LMF is frequently disrupted by genetic factors, age-related problems, medications and metabolic disturbances.<sup>2,3,4</sup>

- Large number of people (almost 20-40%) have a MTHFR genotype variation and are unable to fully convert regular folic acid to LMF.
- Limited absorption results in a significant reduction in the amount of LMF made available to the body; limiting the ability to build and maintain healthy reserves of folic acid and significantly increasing risk of birth defects, homocysteine build up and depression.
- Inability of folic acid to cross the blood brain barrier has also limited its use in the treatment of depression where Folate deficiency has also been found to be widespread.

## Mechanism of action

- Functions as a methyl donor and monoamine synthesis modulator
- Regulates tetrahydrobiopterin (BH4), a critical enzyme cofactor for trimonoamine neurotransmitter synthesis
- Methyl donor for DNA methylation and thus an epigenetic regulator
- Involved in critical enzymatic reactions throughout the body
- By depleting excess homocysteine, folate benefits cardiovascular health and nervous system function



## Clinical applications

The active form of folate, LMF has been linked to benefits of augmenting anti-depressant effect, addressing early memory loss, improving sensation with diabetic peripheral neuropathy and reducing the risks of neural tube defects.

## Infertility and conception support

- LMF Deficiency precipitates hyperhomocysteinemia, a pro-inflammatory state that is linked with poor sperm and oocyte quality, thereby augmenting male and female infertility.
- Supplementation of LMF in periconceptional period has been demonstrated to improve sperm concentration and pregnancy rates in studies involving assisted contraception. Genetic polymorphism of MTHFR enzyme has been observed in infertile couples.
- LMF assures the optimal folate levels for conception in infertile men and women where failure rates are very high.<sup>6,7,8</sup>

## Pregnancy health

Supplementation with folic acid is internationally recommended to women from the moment they are trying to conceive until 12 weeks of pregnancy. Due to the inability of some women to convert folic acid to L-Methylfolate due to gene characteristics, LMF provides an effective folate supplementation during pregnancy for preventing complications in both mother and foetus. which include miscarriages, neural tube defects, congenital heart disease, oral clefts and possibly preterm birth.<sup>9</sup>

## Cardiovascular health

Folate is involved in critical enzymatic reactions throughout the body. Deficiency of folate in the body systems can lead to development of a substance called homocysteine, responsible for cardiovascular decline. LMF benefits cardiovascular health by reducing the levels of homocysteine.<sup>9</sup>

## Diabetic neuropathy

Diabetic peripheral neuropathy (DPN) has been estimated to affect roughly half of all patients with type 2 diabetes mellitus. Elevated levels of homocysteine and reduced bioactivity of nitric oxide induce endothelial dysfunction, endothelial injury, and may impair vasodilation in patients with diabetic neuropathy. LMF has been shown to be more bioavailable and effective in lowering homocysteine levels than naturally occurring folic acid when combined with methylcobalamin and pyridoxal 5 phosphate. In this combination, LMF has been found to be effective for alleviating signs and symptoms of DPN, including anaesthesia, motor neuropathy, and autonomic neuropathy.<sup>10</sup>

## Depressive disorders

Lower systemic levels of folate can result from poor dietary intake, diabetes, various gastrointestinal disorders, hypothyroidism, renal failure, nicotine dependence, alcoholism, and a particular genetic polymorphism prevalent in 70% of depressed patients.

