Statement of the Problem:

What is folic acid?
Folic acid is a B vitamin and an essential nutrient for humans and critical for pregnant women to avoid babies born with birth defects.

Natural folate in food is chemically unstable, especially after cooking and through food preparations.
Folic acid is a chemically stable pro-vitamin that is used in supplements and in food fortification.

Folic acid must be converted to biologically active natural folate within the cell, conversion is slow and variable among individuals.

High intakes of folic acid are associated with unmetabolized folic acid in blood, which is of concern. Very high intakes cause kidney failure.

Solution to the problem:
Needed are stable pro-vitamin folic acid alternatives that can be used in fortification and supplements that are readily metabolized by human cells compared to folic acid.

Here we report the synthesis and biological activity of Di-Formyl Tetrahydrofolate (DiFF) and Methyl,formyl-tertahydrofolate (MeFF) as folic acid alternatives.

Conclusions:
DiFF and MeFF are more chemically stable than the natural folate 5-methyltetrahydrofolate.
DiFF is as stable as folic acid in both food and in solution at 65°C and pH 7.0.
DiFF and MeFF support cell growth at concentrations comparable to the natural folate, 5-formyltetrahydrofolate, and at lower concentrations than folic acid.

Remaining questions:
Do dietary DiFF and MeFF support metabolic health and prevent birth defects in mice?