

Using methanol instead of acetonitrile in an HPLC method should be done with caution – Tips & Suggestions

Methanol is a very common choice for the HPLC mobile phase organic solvent component in Reversed Phase HPLC even though acetonitrile is often superior in several aspects. On the other hand, methanol is often less expensive and less toxic than acetonitrile, so it has advantages as well.

If you wish to simply substitute methanol in place of acetonitrile in a Reversed Phase HPLC method that has already been developed with acetonitrile, you should be aware that methanol is a much weaker solvent than acetonitrile and therefore you will not get the same chromatographic results. For example; if you have a method with 20% acetonitrile and then change it to 20% methanol, you will get longer retention than with the acetonitrile.

Methanol is more polar than acetonitrile so it will increase retention of hydrophobic compounds in Reversed Phase and the **elution** order for some analytes could change as well, especially when a column such as the Cogent Phenyl Hydride™ is used.

For these reasons, changing to methanol should be viewed as a method development tool and not as interchangeable with acetonitrile. Also, for many SOP's changing from acetonitrile to methanol requires internal approval.



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