

Method to Identify Biological Active Substances in a Mixture (Principle¹)

Summary

Methodology for the identification of biological active substances in a mixture without the need for preparative scale chromatography.

Advantages of this methodology include

- Model mixtures can be obtained from the original mixture directly making mixture experiments with unknown, impure substances possible.
- Analysis of the biological activities of the components of an unknown mixture is possible.
- All steps are easy to automate.
- Integration of the analysis of the biological activity of the mixture into HTS process is possible.

Industrial partners and financial investors are sought for various possible commercialisation options.

Background

Which components of an unknown mixture are responsible for the biological activity of the mixture? This is a frequent problem faced in pharmaceutical research, in environmental science and in the chemistry of natural compounds. In order to solve this problem the mixture is usually separated into individual fractions, ideally containing one component, using chromatography. The biological activity of the single fractions is measured and the substances of the active fraction are identified (*Fig. 1*).

¹ A detailed example is described in a separate document.

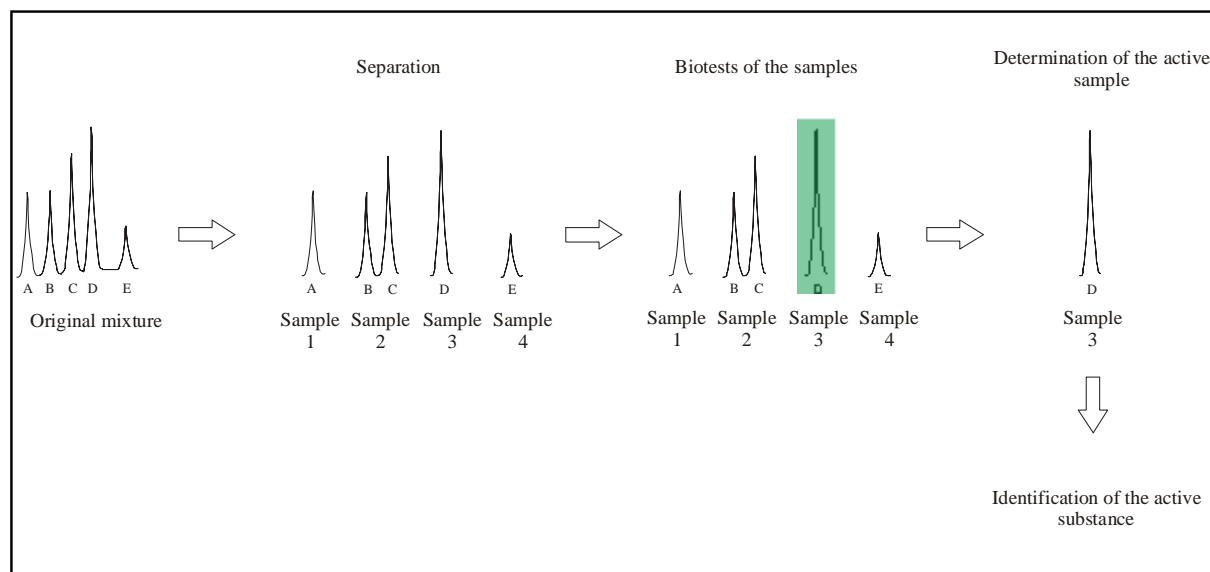


Fig. 1: Common method to determine the active compound of a mixture.

Known problems which may occur using this procedure are as follows.

- Preparative scale chromatography - usually high performance liquid chromatography (HPLC) - is used to obtain the material for biological tests. Unfortunately, selecting a preparative HPLC is often inadequate to obtain pure fractions containing only one substance.
- The quality of the separation using preparative chromatography depends on the kind of mixture and also the experience of the chemist performing the HPLC. Thus, the separation is difficult to automate and to integrate in high throughput screening (HTS) processes.
- As each component of the mixture is tested separately, interactions between the mixture components (synergies and antagonisms) are not indicated. So the measured effect of a substance in a component may differ from the effect of the substance in the original mixture.

FESTEL CAPITAL is supporting the commercialisation of this innovative methodology for the identification of biological active substances.

Description

For the identification of the active compounds the mixture is divided into a number of equal samples. These samples are treated with various adsorbents (each sample is treated with a different adsorbent) resulting in a number of samples (called sub-

mixture in the following) which differ in their component pattern. These patterns are linear independent caused by non-linear events during the adsorption procedure.

Each of these sub-mixtures is divided into two parts. One part is used for a fingerprint analysis (the fingerprints contain information about the compound content in the sub-mixtures). The other part is used to measure the biological activity.

The measured biological effects are related to the compound content in the sub-mixtures by means of correlation analysis. As a result of the statistical analysis, information on the peak in the fingerprint is obtained which represents the active compound of the mixture, thus, making known the position of the biological active substance. With this information it is possible to identify the biological active substance directly from the mixture (*Fig. 2*).

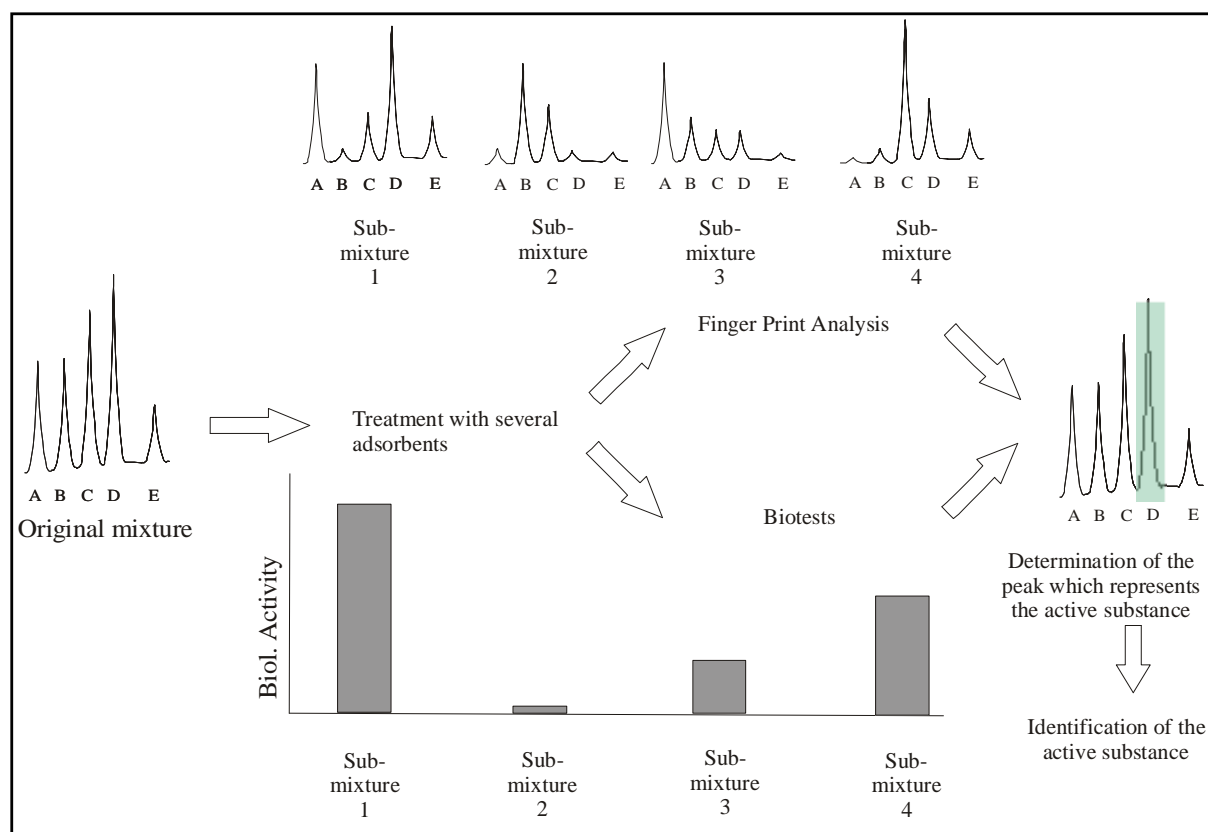


Fig. 2: Suggested method to determine the active compound of a mixture.

Advantages

- A separation of the mixture using preparative chromatography to obtain the samples for the biological tests is not necessary. To obtain the fingerprints of the com-

position of the sub-mixtures the most adequate analytical method can be used (analytical HPLC, gas chromatography, spectroscopic methods).

- It is necessary to perform the treatment of the original mixture with adsorbents (to obtain the sub-mixtures) via the solid phase extraction (SPE) technology in micro-titer plate scale. Such SPE systems have been designed for the use in automatic sample preparation procedures. Also all other steps of the described method (fingerprint analysis, biological tests) are easy to automate, thus making it possible to integrate the analysis of the biological activity of a mixture into HTS processes.
- The obtained data set contains also the information about the interactions between the compounds of the mixture concerning the biological target. If this data set shows a good quality, a further data analysis to predict the behaviour of the active compounds in real mixtures will be possible (similar to well-known mixture experiments)

Investment Opportunity

The aim of FESTEL CAPITAL is to commercialize this innovative methodology. In the search for industrial partners different commercialization options, such as out-licencing or a sale of all relevant intellectual property and know-how, are possible. Detailed information can be provided after the signing of a confidentiality agreement.

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About FESTEL CAPITAL

FESTEL CAPITAL is an advisory and investment firm focusing on the commercialisation of technologies in the areas of energy, environment, health, materials and nutrition.

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