

SUPPLEMENTARY MATERIAL

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1 MATLAB simulation code

A schematic representation of all the stages needed for the complete method development is reported in Fig. 1.

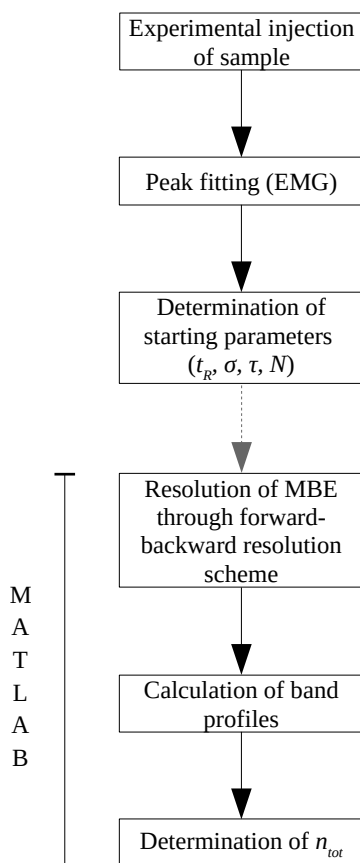


Fig. 1: Schematic representation of the method development steps.

More in detail, the parameters needed for the theoretical prediction of band profiles are: retention time (t_R), standard deviation (σ), time constant of exponential decay function (τ) and plate number (N). They have been obtained by fitting experimental peaks with an EMG function (see main text for details). As an example, the result of peak fitting applied to the *Cannabis* extract is reported in Fig. 2.

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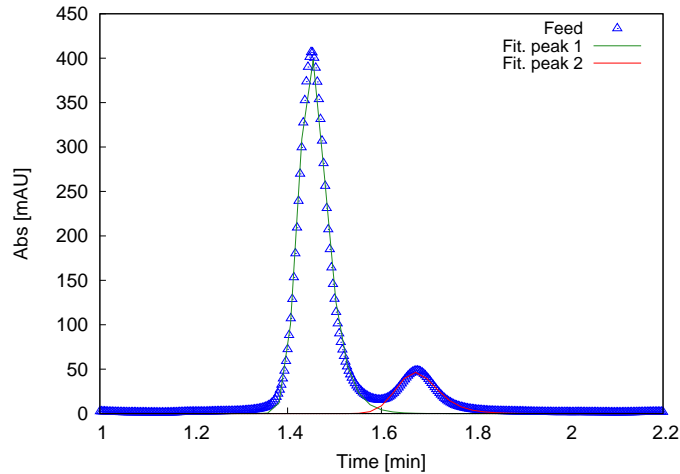


Fig. 2: Peak fitting with EMG function applied to *Cannabis* extract. First peak: CBD, second peak: CBC and THC.

Then a MATLAB code has been used for the calculation of band profiles in recycling chromatography, based on the number of column passages (n), using a forward-backward differences scheme for obtaining numerical solutions of the Equilibrium-Dispersive (ED) Model of chromatography [1] (see main text for details). Results are reported in Fig. 3 for $n=5$ that corresponds to a number of switches $n_s=3$, since 2 columns are used. If the recycling process is performed on one column, only $n=4$ column passages are allowed in order to avoid the “re-mixing” of the two peaks. Otherwise, the use of APR (two columns) allows one more passage through column. Indeed, the two columns are connected in series, so what elutes from upstream column is directly injected into downstream column, without any switch, before leaving the system.

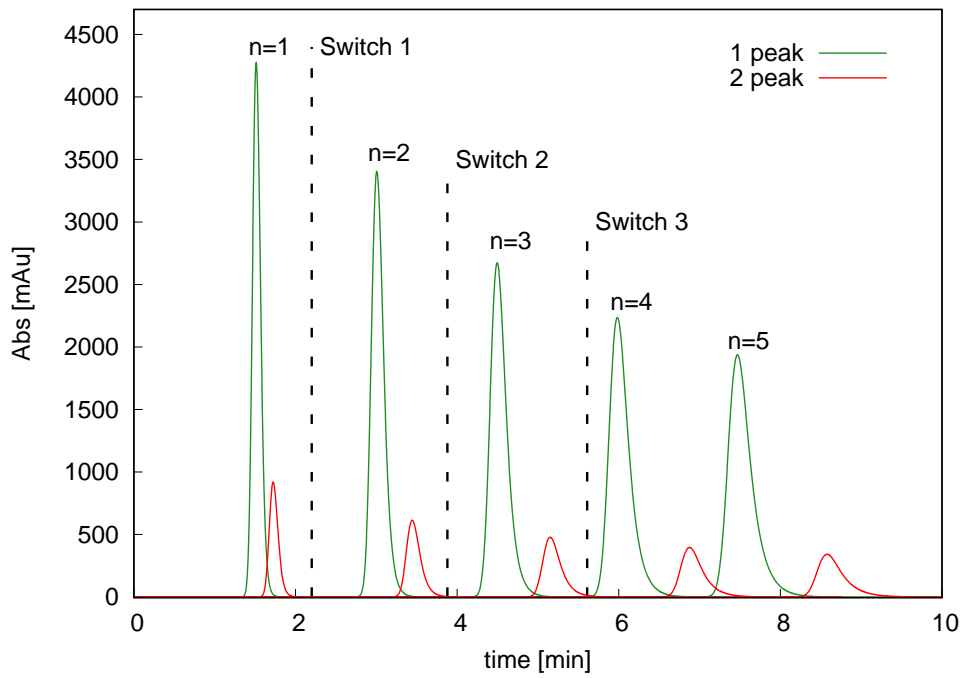


Fig. 3: Theoretical prediction of band profiles using MATLAB code for $n=5$.

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231 **2 Offline analysis**

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233 Fig. 4 shows offline analysis of recycling fractions using analytical method described
234 in [5]. See Fig. 4 of the main text for the identification of the two fractions.

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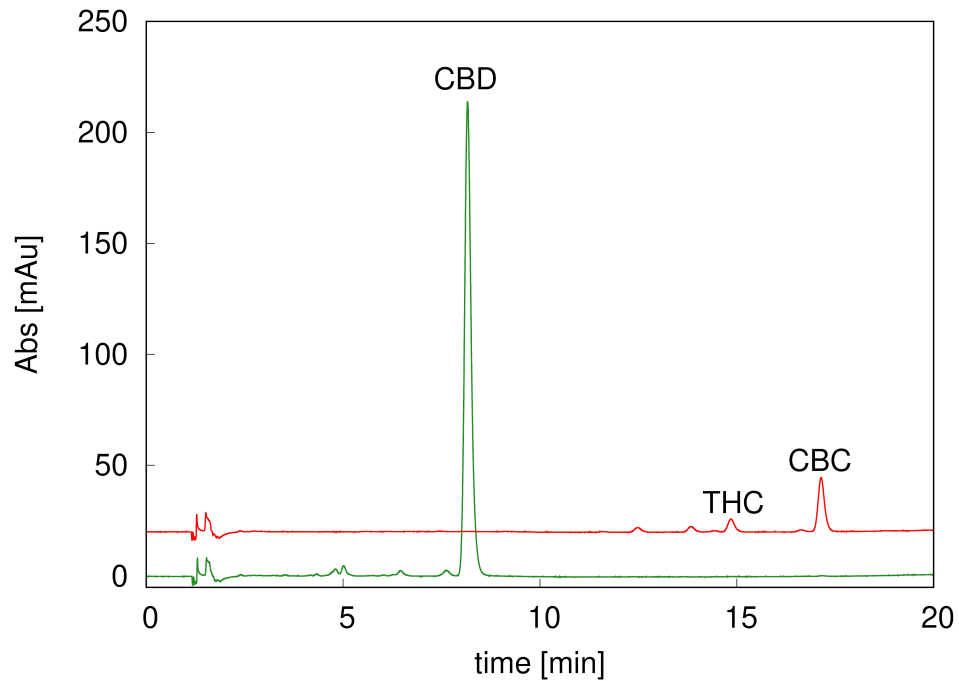
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258 **Fig. 4:** Offline analysis of recycling fractions. In green the chromatogram of first
259 fraction and in red the chromatogram of second fraction.

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3 Batch chromatography

3.1 100% EtOH

Fig. 5 shows a batch chromatogram obtained by injecting 20 μL of *Cannabis* sample in a C18 150 \times 8 mm column using 100% ethanol as mobile phase.

The fractions collected from the batch were analyzed offline using analytical method reported in [5]. Then, purity, recovery, productivity and solvent consumption have been calculated for cases B and C reported in Table 2 of the main text.

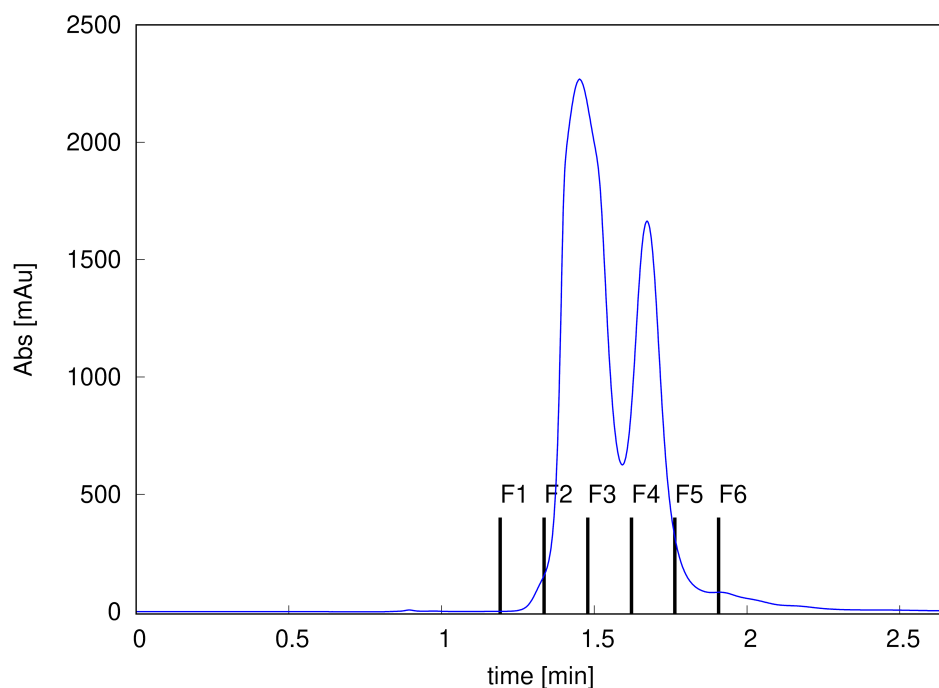
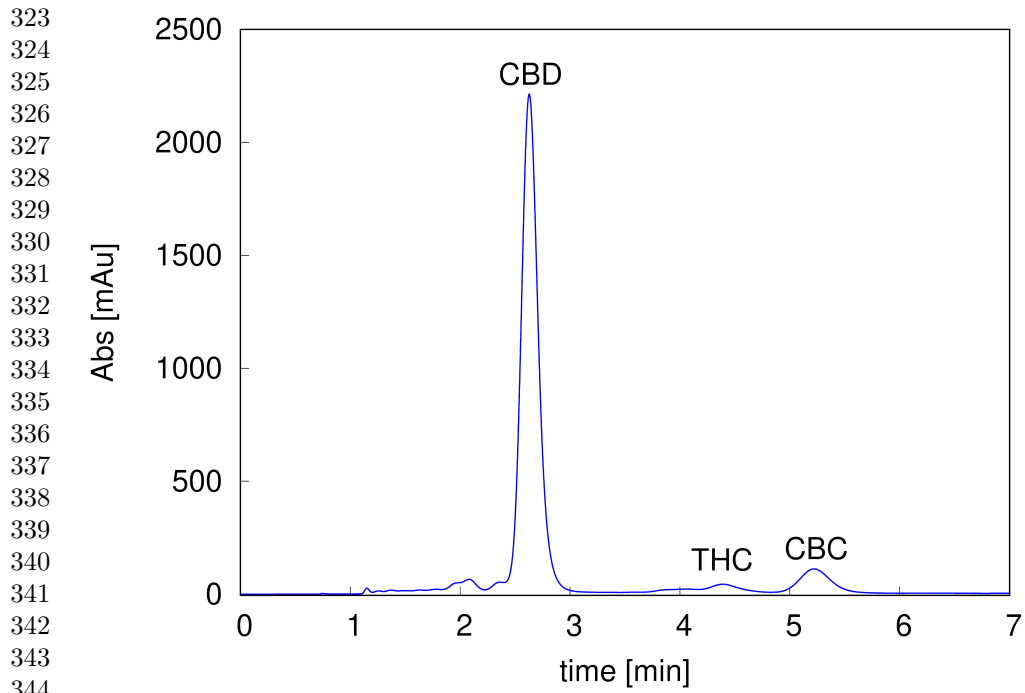


Fig. 5: Batch chromatogram of 20 μL injection of *Cannabis* sample using 100 % ethanol as mobile phase.. Collected fractions are indicated with increasing numbers (F1-F6).

3.2 80% EtOH

Fig. 6 shows a batch chromatogram obtained by injecting 20 μL of *Cannabis* sample in a C18 150 \times 8 mm column using 80/20 % ethanol/water as mobile phase to obtain the baseline separation between the peaks of CBD and THC.

The CBD peak has been collected and purity, recovery, productivity and solvent consumption have been calculated for case E in Table 2 of the main text.



345 **Fig. 6:** Batch chromatogram of 20 μL injection of *Cannabis* sample using 80/20 %
346 ethanol/water as mobile phase.

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