

# Supplementary Materials: Scale-Up Synthesis and In Vivo Anti-Tumor Activity of Curcumin Diethyl Disuccinate, an Ester Prodrug of Curcumin, in HepG2-Xenograft Mice

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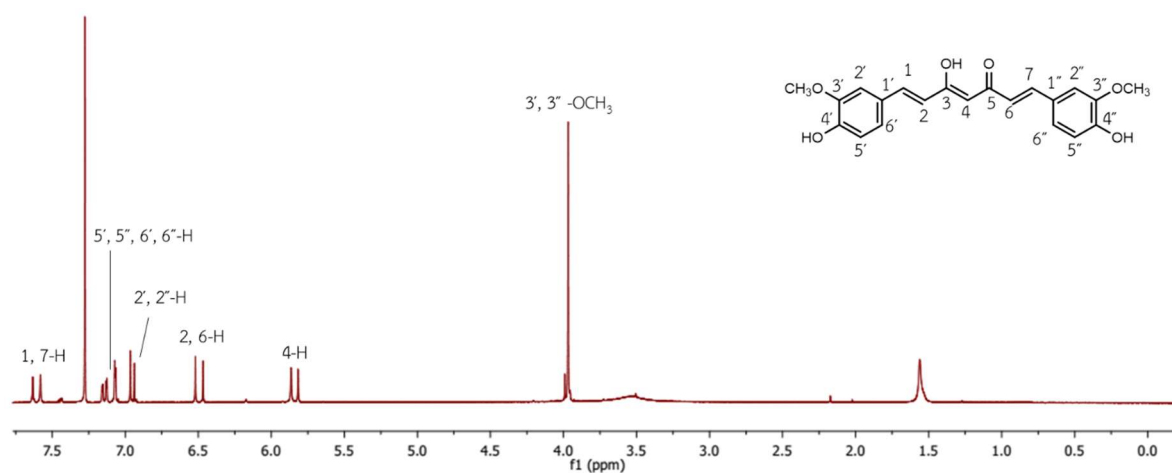


Figure S1.  $^1\text{H-NMR}$  spectrum of curcumin.

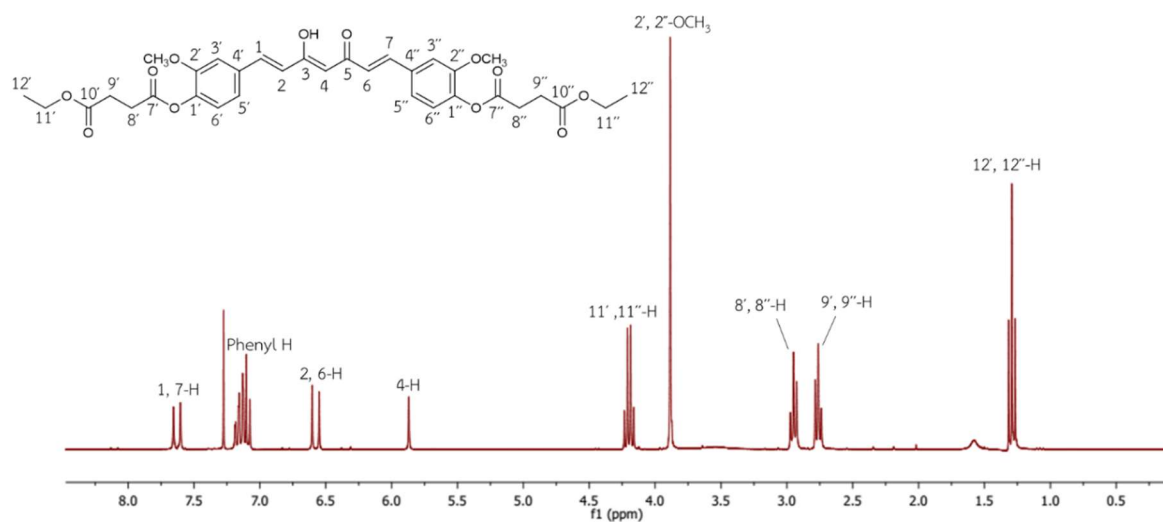
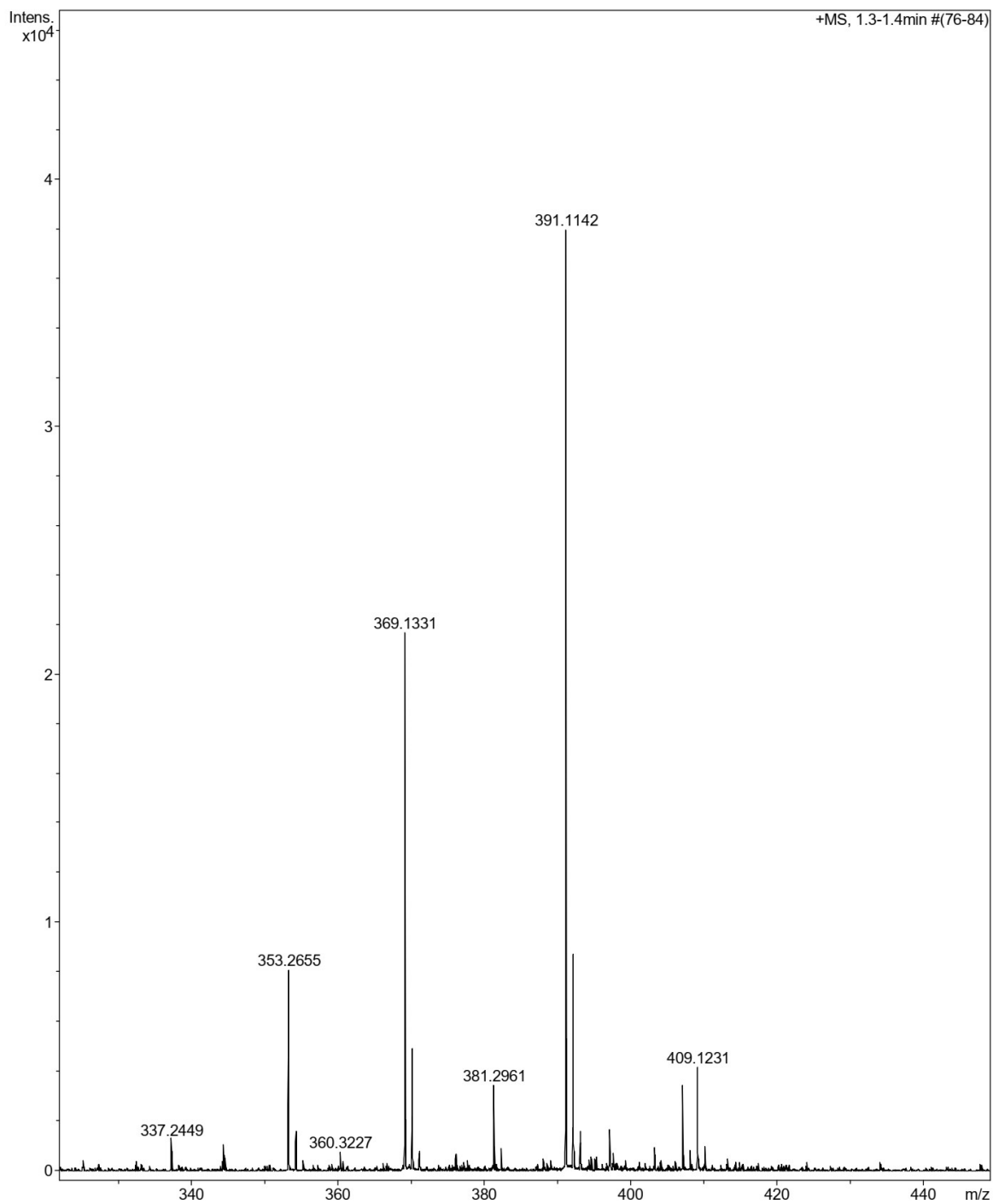
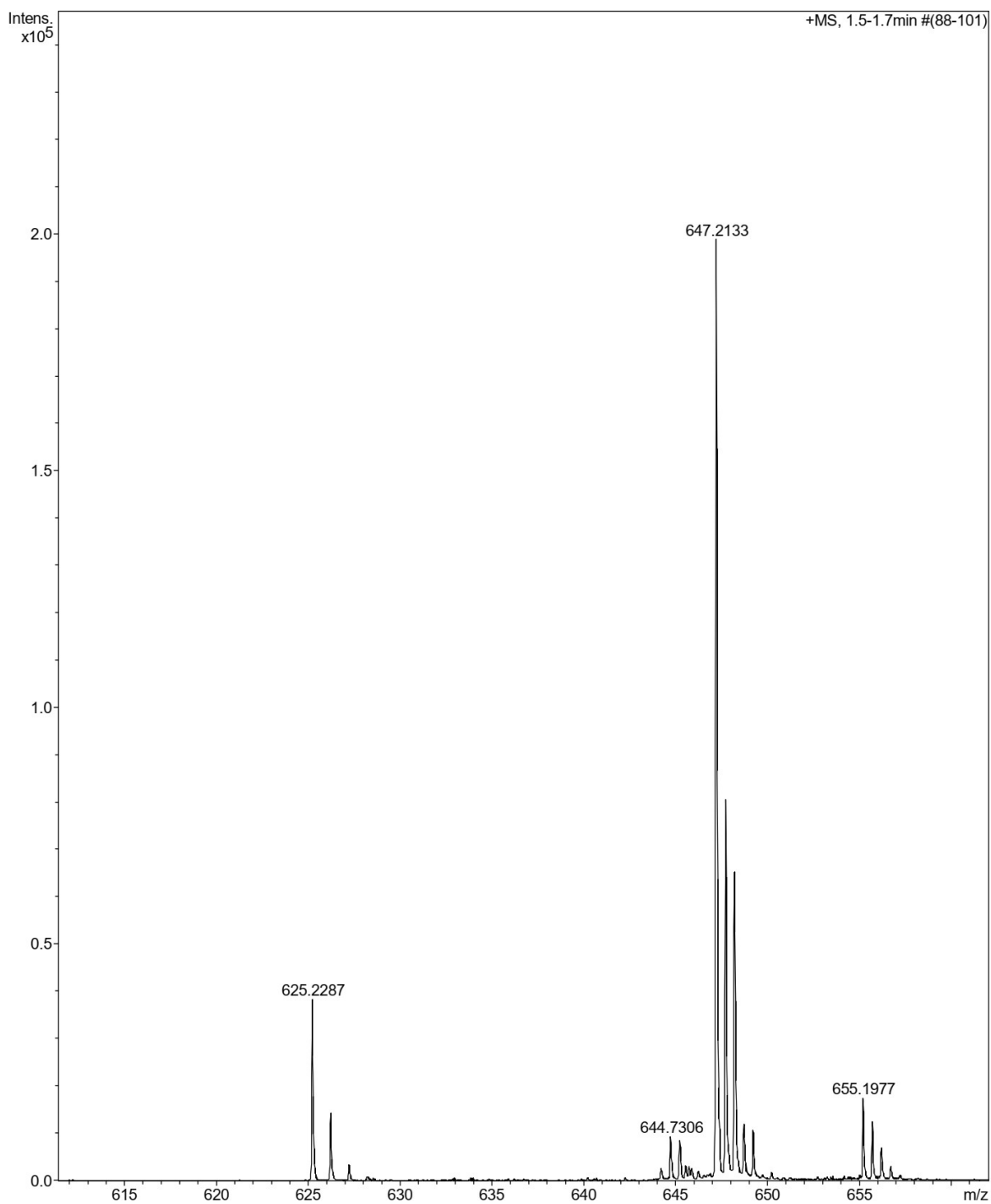


Figure S2.  $^1\text{H-NMR}$  spectrum of curcumin diethyl disuccinate.



**Figure S3.** Mass spectrum of curcumin.



**Figure S4.** Mass spectrum of curcumin diethyl disuccinate.

#### **Determination of chromatographic purity of the prepared curcumin and CurDD**

The prepared curcumin and CurDD were injected into an ultra-high performance liquid chromatographic system to determine chromatographic purity. The chromatographic conditions for the assay were described below.

	Initial (0 min) – A:B = 55:45
Mobile phase	2 min – A:B = 50:50
A = 0.2 % Formic acid in water	2.5 min – A:B = 50:50
B = Acetonitrile	5.0 min – A:B = 25:75
	5.5 min – A:B = 55:45
	7 min – A:B = 55:45
Column	Acquity UPLC BEC C18 (50 mm x 2.1 mm, 1.7 $\mu$ m)
Flow rate	0.5 mL/min
Column oven temperature	35 $^{\circ}$ C
Injection volume	2 $\mu$ L
Detection wavelength	$\lambda$ = 400 nm for CurDD, 425 nm for curcumin

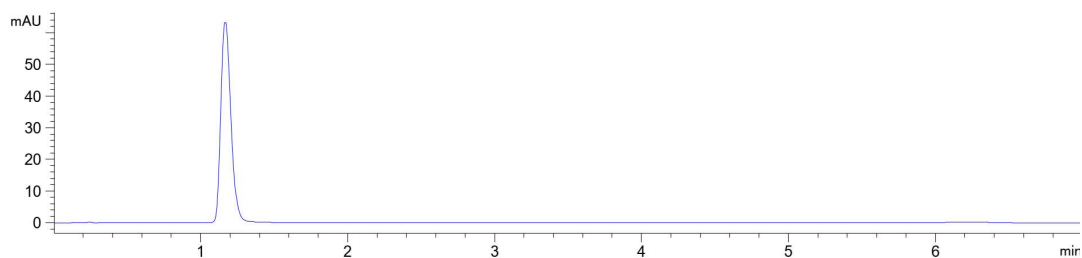


Figure S5. UHPLC chromatogram of curcumin.

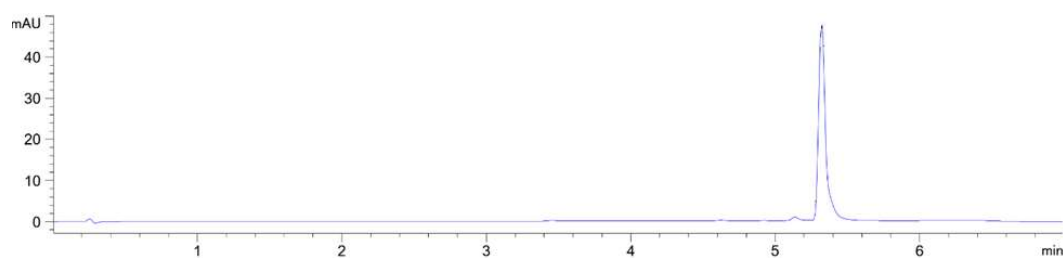


Figure S6. UHPLC chromatogram of curcumin diethyl disuccinate.

### Curcumin (Coupled TwoTheta/Theta)

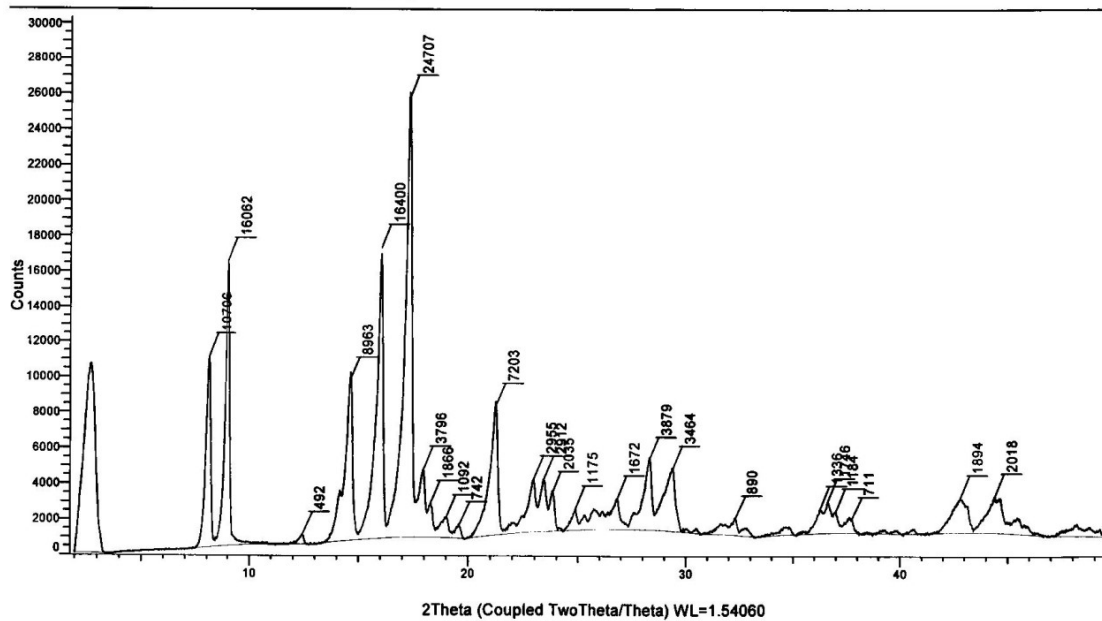


Figure S7. Powder X-ray diffraction spectrum of curcumin.

CDD (Coupled TwoTheta/Theta)

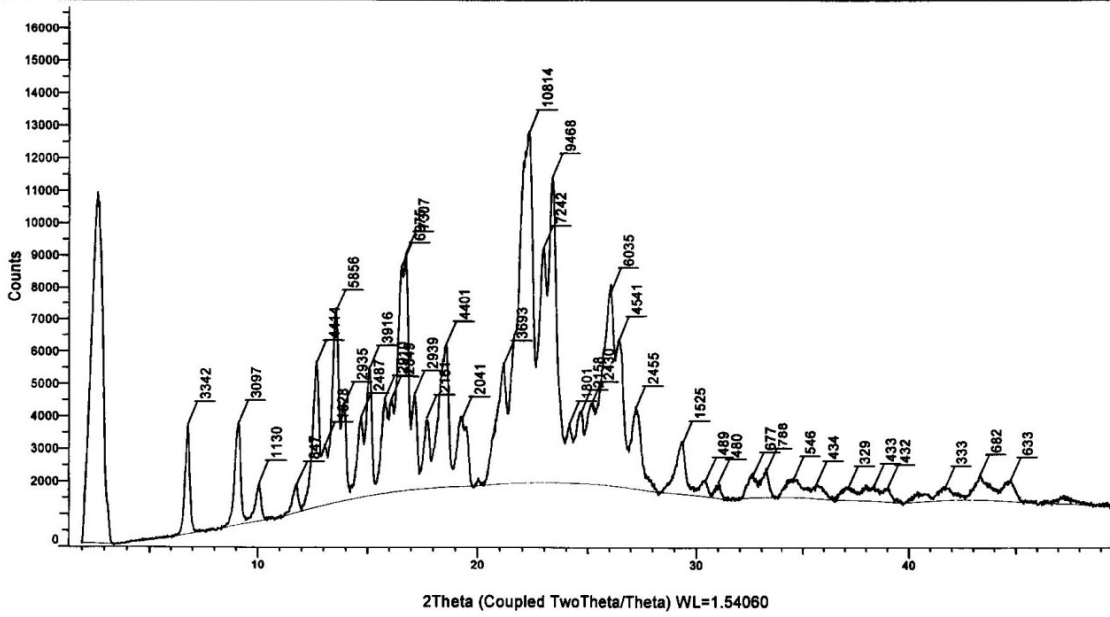


Figure S8. Powder X-ray diffraction spectrum of CurDD.

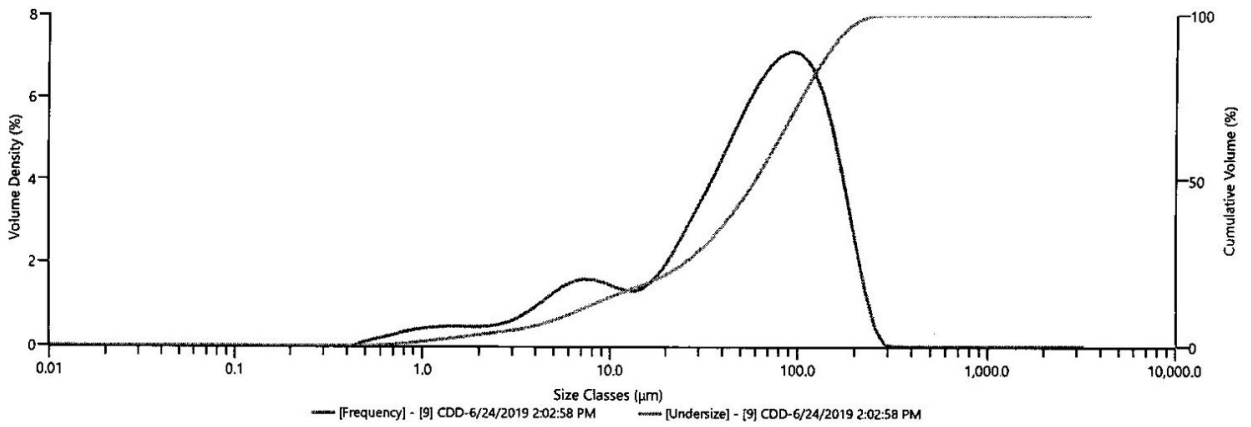


Figure S9. Particle size distribution analysis by laser diffraction of CurDD.

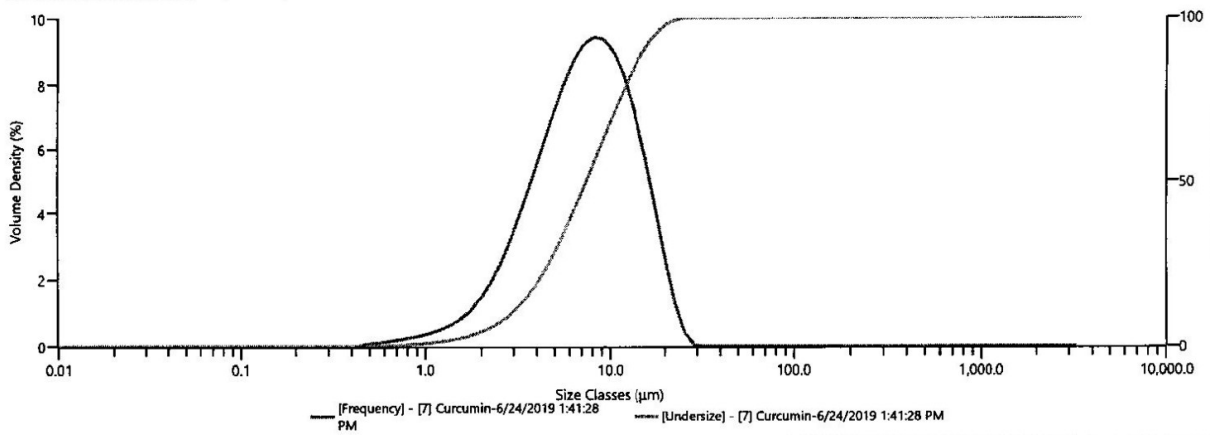


Figure S10. Particle size distribution analysis by laser diffraction of curcumin.