# SUPPORTING INFORMATION

# Curcumin-derived green plasticizers for Poly(vinyl) chloride

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## 1. General Remarks:

Reagent grade Chloroform, HPLC grade tetrahydrofuran, methylene chloride, N,N-dimethylformamide, ethylacetate were used without further purification. Curcumin >98%, Stearic Acid 97%, 4-Dimethylaminopyridine (DMAP) 99%, Dibutyl Phthalate (DBP) 98%, were obtained from Acros Organics. Silica gel 60 F 254 plates for thin-layer chromatography (TLC) were purchased from Fisher Scientific. Column chromatographic separations were performed using silica gel (Fisher) with a particle size of 0.040-0.063 mm. Nuclear magnetic resonance (NMR) spectra were recorded on Oxford NMR 600 (600 MHz) spectrometer. Mass spectra (ES-MS) were recorded using an Agilent LC/MS mass spectrometer. Thermogravimetric Analysis was done using Thermo Gravimetric Analyzer TA Instruments (2950). Differential Scanning Calorimetry was performed using Differential Scanning Calorimeter TA Instrument Q2000. The FTIR spectra was collected using a Bomem-MB102 spectrometer, and was acquired in the range of 4000 and 650 $cm^{-1}$ at a resolution of 4 $cm^{-1}$.

## 2. General Procedure Synthesis:

### 2.1. (Typical synthetic procedure via the high atom economy route) Synthesis of 4,4'-((1*E*,6*E*)-3,5-dioxohepta-1,6-diene-1,7-diyl)bis(2-methoxy-4,1-phenylene) distearate. Curcumin distearate (Cu18) (0.550 g, 57%).

In a 50 mL round bottom flask, Curcumin (1.36 mmole, 500 mg), Stearic Acid (2.2 mmole, 851.6 mg), and Acetic Anhydride (1.36

mmole, 1.5 mL) were added and swirled, followed by addition of DMAP (2 %mmole, 6.63 mg) at room temperature. The flask was allowed to heat to 50°C in oil bath; at this point the solution became orange. After 24 hours, 29 μL of Millipore water was added to the solution and allowed to stir for one hour at 90°C and under high vacuum. After the reaction was stopped, it was dissolved in methylene chloride and washed with $NaHCO_3$ (pH 8.3), and one time with Brine solution. Solution was then dried with sodium sulfate, filtered and excess solvent evaporated. The product was then passed through a silica gel column in chloroform, using 92:8 $CH_2Cl_2$:EtoAc as eluent. The second band was collected and it was shown to be the final product as indicated by NMR spectroscopy.

$\delta_{H\ NMR}$ (600MHz; $CDCl_3$; $Me_4Si$): 0.87-0.89 (6H, t, -RC*H*$_3$); 1.28-1.36 (52H, m, [-C*H*$_2$-]n); 1.40-1.44 (4H, m, ) 1.75-1.78 (4H, t, $COCH_2CH_2R$ ); 2.57-2.60 (4H, t, C*H*$_2$COR ); 3.87 (6H, s, ROC*H*$_3$ ); 5.86 (2H, s, $(CO)_2CH_2$); 6.55-6.58 (2H, d, Ar); 7.04-7.26 (6H, m, Ar); 7.61-7.63 (2H, d, Ar). $\delta_{C\ NMR}$ (600MHz; $CDCl_3$; $Me_4Si$), δ (ppm): 14.12; 22.69; 25.00; 31.92; 34.03; 55.89; 101.75; 111.42; 121.09; 123.30; 124.15; 133.80; 139.99; 141.45; 151.43; 171.64; 183.08. MS (ESI) calcd. for $C_{57}H_{88}O_8$ : 900.6; found: 901.6 [M+H]+. FT-IR ($cm^{-1}$): 2917, 2843, 2365, 1760 (ester C=O stretch), 1601(C=O stretch)

**2.2. (Typical synthetic procedure via the acid chloride route) Synthesis of 4,4'-((1E,6E)-3,5-dioxohepta-1,6-diene-1,7-diyl)bis(2-methoxy-4,1-phenylene) dioctanoate. Curcumin dioctanoate (CuC8). (270 mg, 32%).**

In a double neck 250mL r. b. flask, octanoic acid (4.3mL, 27.14mmol) was dissolved in 15mL of DCM. The flask was degassed and a continuous flow of N2 was set into the reaction mixture. Oxalyl chloride (7.16mL, 81.43mmol) was then added dropwise to the reaction, followed by two drops of catalytic DMF. Solution was allowed to stir at room temperature for 3 hours. Solvent and excess oxalyl chloride were removed from flask in the rotovap.

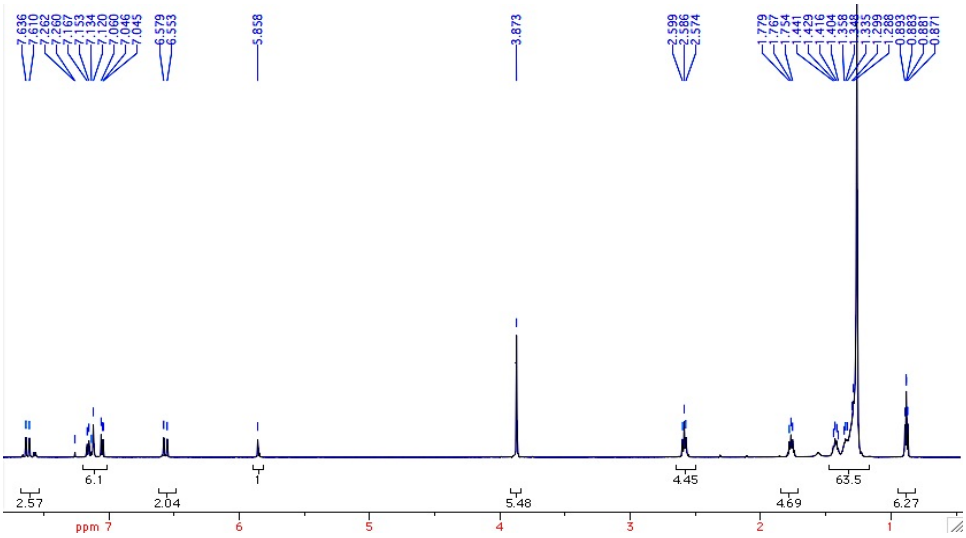
In a 250mL 2-neck round bottom flask, Curcumin (2000mg, 5.42mmol) and DMAP (1655mg, 13.57mmol) were dissolved in 50ml of dry DMF at Room Temperature. Et3N (2.30m, 16.28mmol) was added to the mixture dropwise, degassed with N2, and allowed to stir for 3 minutes. The first reaction containing *octanoyl chloride* was added to this mixture and allowed to stir for 20.5 hours at 71oC. An extra 30mL of dry DMF was added to the mixture before the temperature reached 71$^{o}$C. The product was passed through a silica gel column in dichloromethane, using 100 mL of 98:2 $CH_2Cl_2$:Methanol as eluent. The first band was collected and it was shown to be the final product as indicated by NMR spectroscopy.

$\delta_{H\ NMR}$ (600MHz; $CDCl_3$; $Me_4Si$): 0.87-0.91 (6H, t, -RC*H*$_3$); 1.30-1.46 (16H, m, [-C*H*$_2$-]n); 1.73-1.80 (4H, m, ) 2.50-2.62 (4H, t, $COCH_2CH_2R$ ); 3.87 (6H, s, ROC*H*$_3$ ); 5.86 (2H, s, $(CO)_2CH_2$); 6.55-6.60 (2H, d, Ar); 7.04-7.22 (6H, m, Ar); 7.60-7.65 (2H, d, Ar). $\delta_{C\ NMR}$ (600MHz; $CDCl_3$; $Me_4Si$), δ (ppm): 14.05; 22.54; 25.04; 28.94; 31.64; 34.01; 55.85; 101.75; 111.41; 121.26; 124.15; 129.17; 133.81; 139.93; 141.46; 151.48; 171.61; 183.09. FT-IR ($cm^{-1}$): 2917, 2843, 2356, 1765 (ester C=O stretch), 1730(C=O stretch).

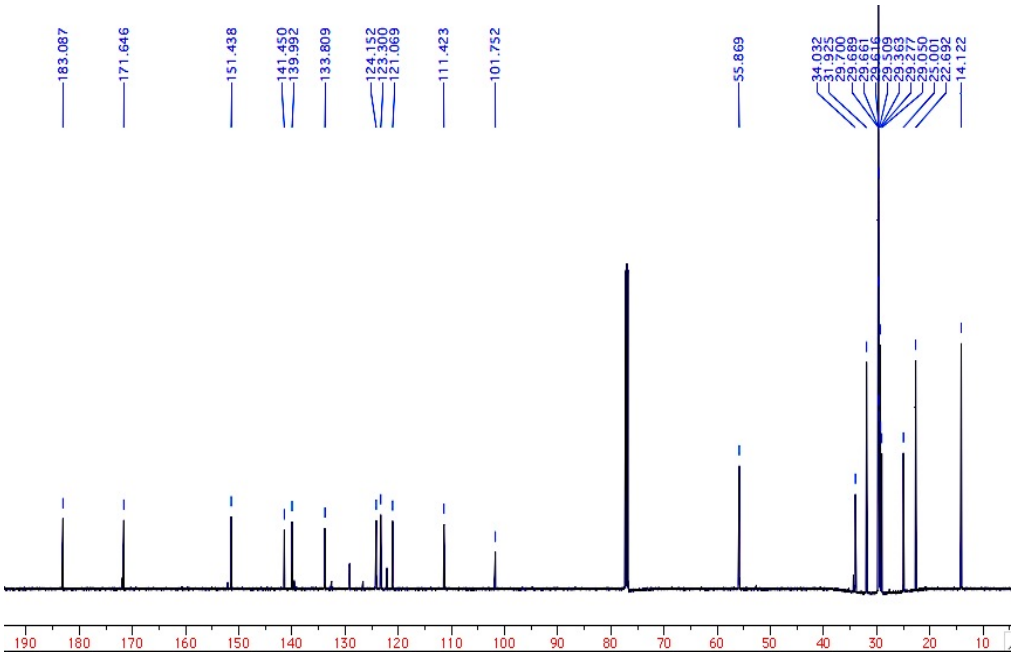
## 3. Spectral Data of Compounds

### 3.1. 4,4'-((1*E*,6*E*)-3,5-dioxohepta-1,6-diene-1,7-diyl)bis(2-methoxy-4,1-phenylene) distearate: Curcumin distearate (Cu_C18).

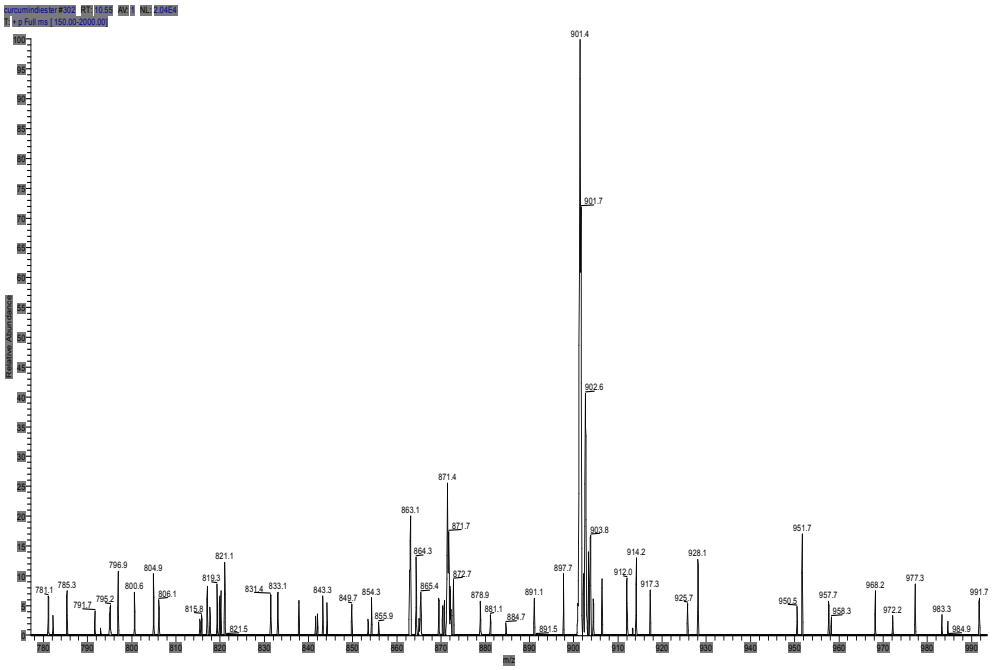
#### 3.1.1. $^1$H NMR:



### 3.1.2 $^{13}$C NMR:

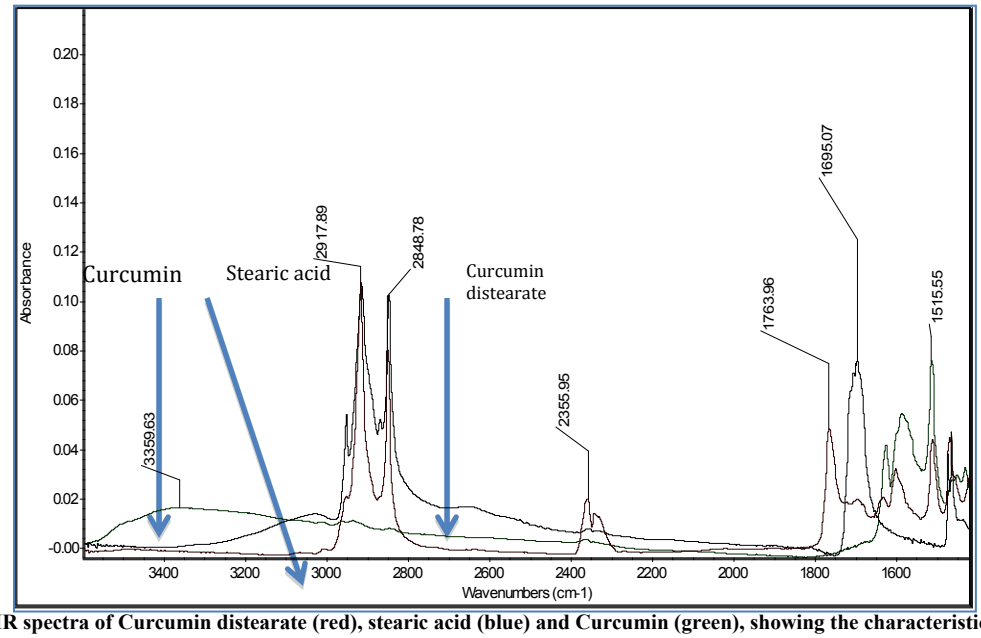



### 3.1.3 Mass Spectrogram:



### 3.1.4 FTIR Spectrum

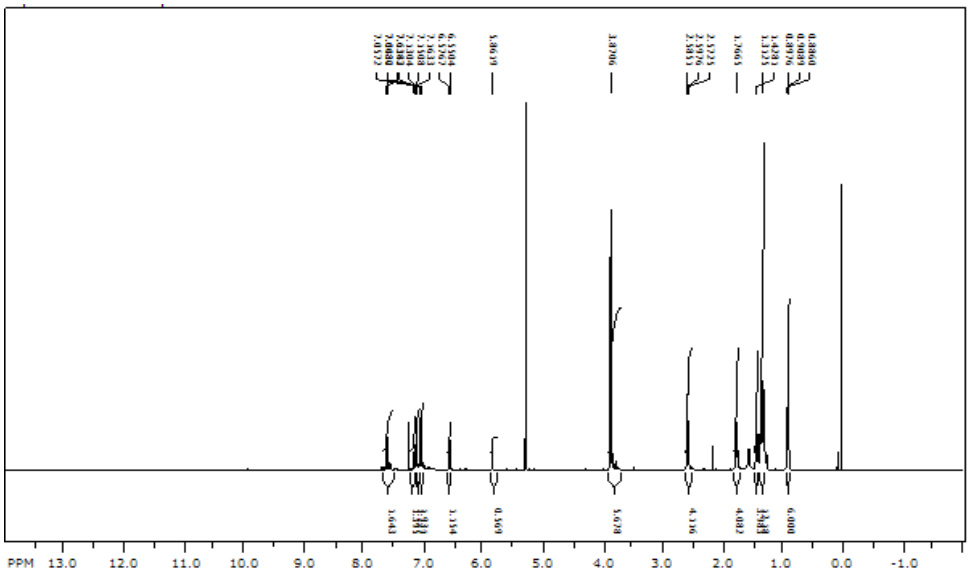
**4.**



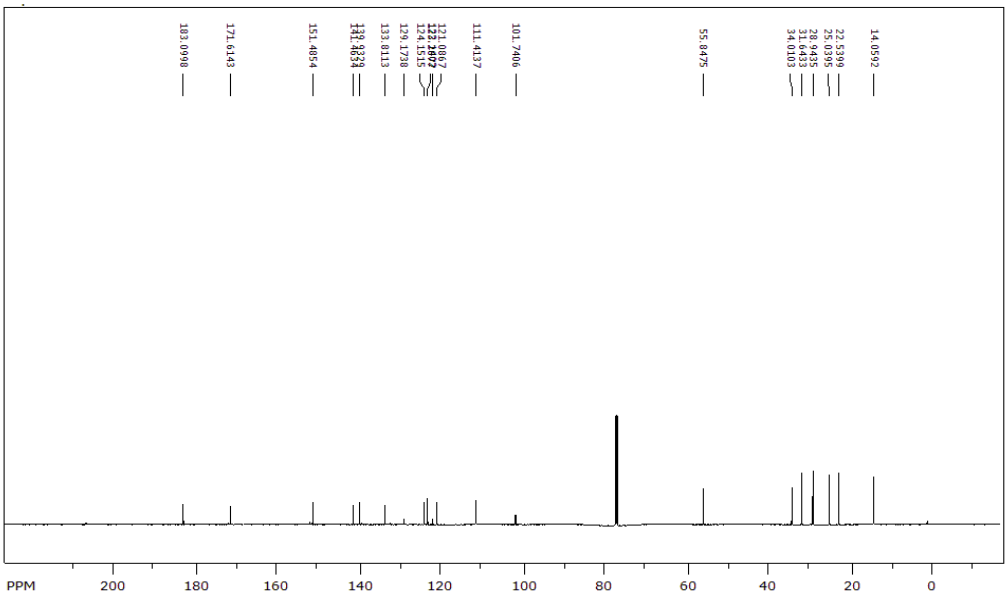

**FTIR spectra of Curcumin distearate (red), stearic acid (blue) and Curcumin (green), showing the characteristic absorption peaks.**

## 3.2 Synthesis of 4,4'-((1E,6E)-3,5-dioxohepta-1,6-diene-1,7-diyl)bis(2-methoxy-4,1-phenylene) dioctanoate. Curcumin dioctanoate (CuC8).

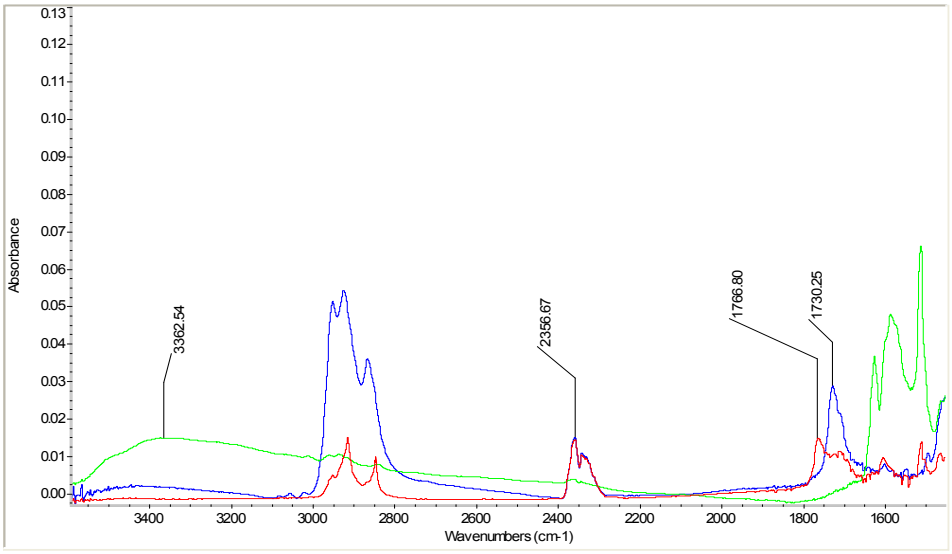
### 3.2.1 $^{1}$H NMR:



### 3.2.2 $^{13}$C NMR:

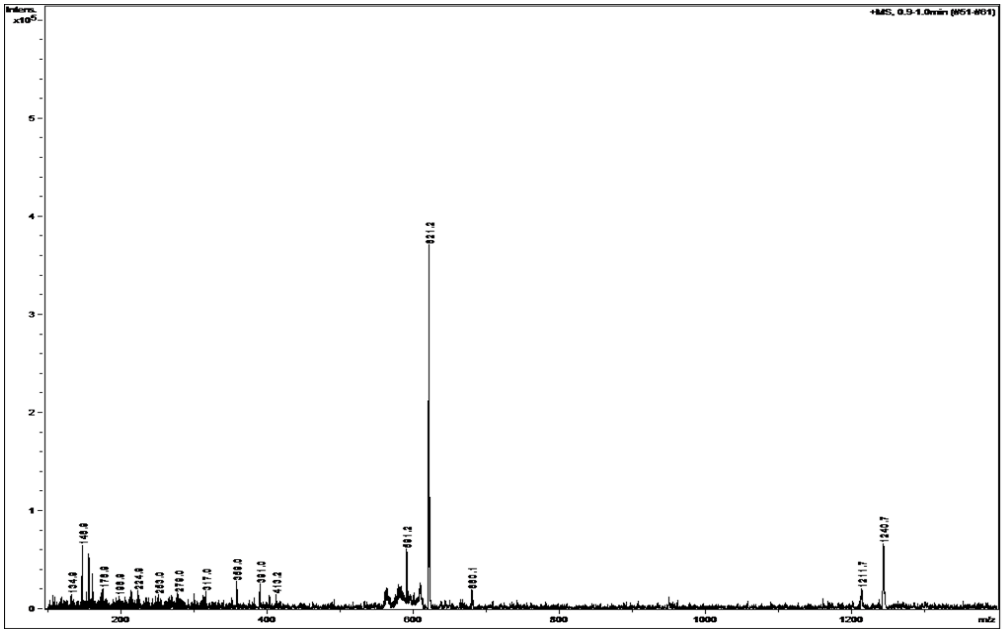



### 3.2.3 FT-IR:




FTIR spectra of Curcumin dioctanoate (red), octanoic acid (blue) and Curcumin (green), showing the characteristic absorption peaks.

### 3.2.4 Mass Spectrogram :



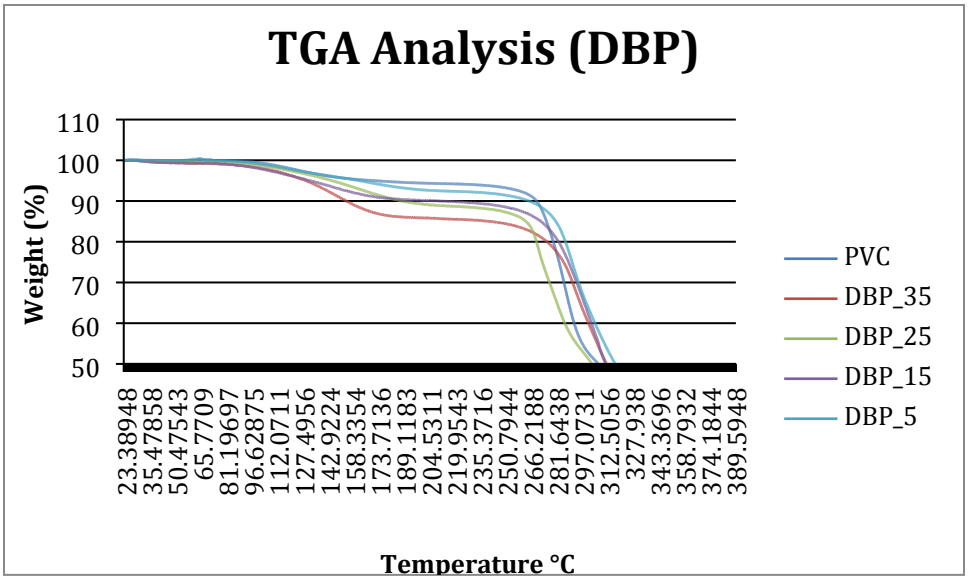
## 4. Plasticization method:

The solvent-casting method was used to make the PVC:Cu18 plastic films at different percent weights: 5, 15, 25, and 35% of plasticizer (w/w) to PVC. PVC and the desired amount of plasticizer (total weight ~25 mg) were added to a 10 mL vial, followed by the addition of tetrahydrofuran (THF) (3 mL). The mixture was agitated and heated to 35$^{o}$C until a homogenous solution was obtained. Residual THF was removed at room temperature for 72 hours and then films were dried further in vacuum oven at 45$^{o}$C for 72 hours.

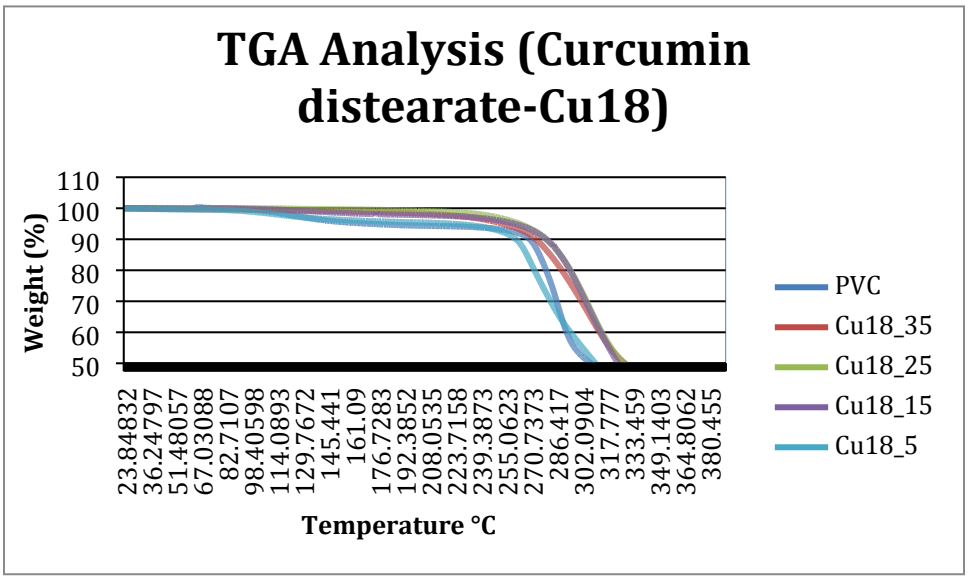
The PVC:DBP (control) were made using the same procedure.

## 5. Thermogravimetric Analysis (TGA)

. A Thermo Gravimetric Analyzer TA Instruments (2950) was used for thermogravimetric (TGA) characterization. Soft PVC samples were heated from room temperature to 800 $^{o}$C at 10 $^{o}$C /min in nitrogen atmosphere.




**TG A analysis of unplasticized PVC (blue) and plasticized PVC with: 5% (w/w) (light blue), 15% (w/w) (purple), 25% (w/w) (green), and 35% (w/w) (red) DBP.**

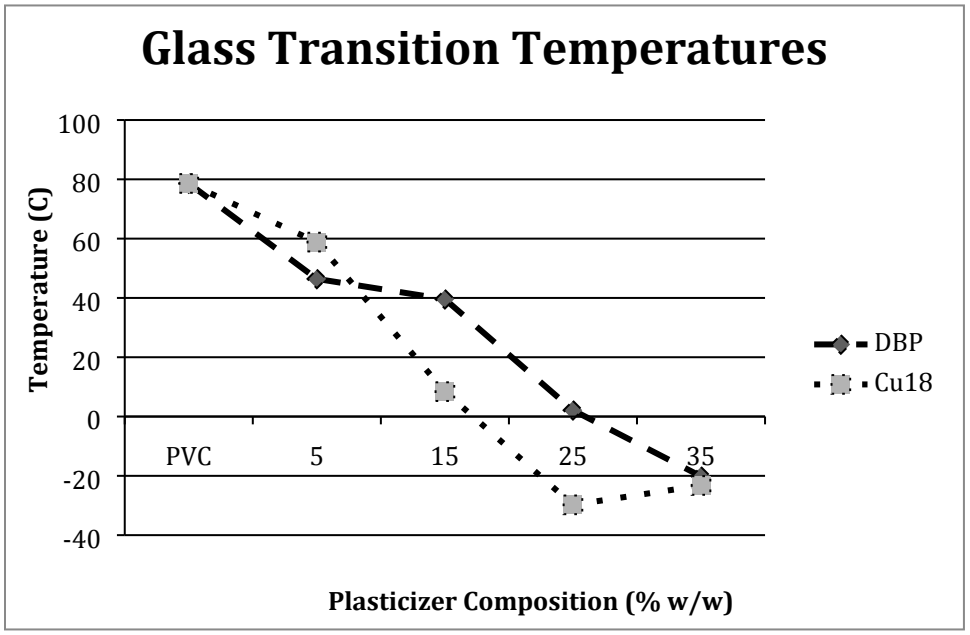



**TG A analysis of unplasticized PVC (dark blue) and plasticized PVC with: 5% (w/w) (light blue), 15% (w/w) (purple), 25%(w/w) (green), 35%(w/w) (red) DBP.**

## 6. Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) tests were performed on a DSC-TA Instrument Q2000, heating soft PVC samples between 30°C and 80°C at 10 °C /min, then cooling back to -70 °C at 10 °C /min, followed by a second heating

step at 10°C to 120°C. Only the second heating step was considered representative in order to calculate the glass transition temperature of materials.




## 7. Plasticized PVC films

### 7.1. Sample weights for Leaching Experiment

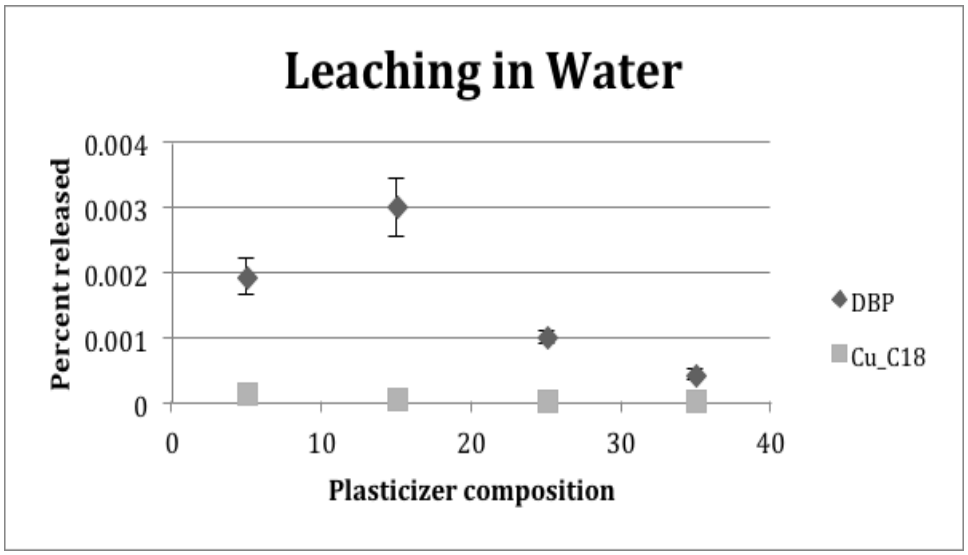
| | | Sample Weight mg | Plasticizer weight mg |
|---|---|---|---|
| **Water:Cu18** | **5%** | 26.3 | 1.315 |
| **Water:Cu18** | **15%** | 26 | 3.9 |
| **Water:Cu18** | **25%** | 25.1 | 6.275 |
| **Water:Cu18** | **35%** | 25.3 | 8.855 |
| | | | |
| **Water:DBP** | **5%** | 25.5 | 1.275 |
| **Water:DBP** | **15%** | 25.1 | 3.765 |
| **Water:DBP** | **25%** | 25 | 6.25 |
| **Water:DBP** | **35%** | 26.2 | 9.17 |

Table 1. Sample weights for leaching experiment in water

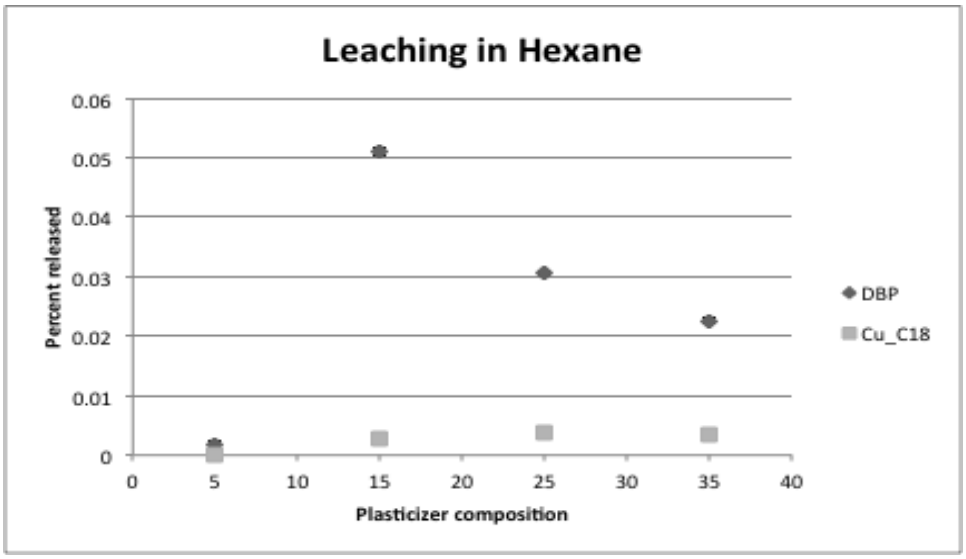
### 7.2. Leaching experiment setup

Leaching of plasticizers from plasticized PVC samples was studied by placing thin rectangular samples (approximately 3 x 1 $mm^2$) weighing ~25-26 mg in 5 mL of deionized water or *n*-Hexane in 10ml glass vials. To enhance the effect of leaching, so that observations could be made in a short-time period, the temperature of the oven was elevated to 50°C. After 7 days, the amount of plasticizer leached was assayed spectrophotometrically using a UV Vis spectrophotometer at 280 nm, for DBP, and 430 nm for Curcumin distearate. The values reported are the average of three determinations.

### 7.3 Leaching results




**UV-Vis analysis results for leaching of different plasticizer compositions in *n*-Hexane for 7 days at 50 C. Data are presented as mean±SE (n=6 replicates. Significant differences between plasticizers at different concentrations and control are indicated as ***p<<0.0001 (Student's t-test)**




**UV-Vis analysis results for leaching of different plasticizer compositions in *n*-Hexane for 7 days at 50 C. Data are presented as mean±SE (n=6 replicates. Significant differences between plasticizers at different concentrations and control are indicated as ***p<<0.0001 (Student's t-test)**

## 8. MTT Assay for Cell Viability

A cervix cell line, Hela, was cultured in a 96-wells microplate in 100 µL medium containing about 5000 cells seeded into each wells. After an overnight incubation for attaching, medium was removed and another 100 µL of medium containing the plasticizer sample, diluted with 1 mL v/v% dimethylsulfoxide (DMSO), was added to make the final concentrations of 0, 0.0625, 0.125, 0.25 and 0.5 mg/mL. Wells containing normal medium were used as control. After incubation for 24 hours, 10 µL of MTT was added into the wells and incubated in a humidified environment of 5% CO⁻2 and 37oC for 2hours. The medium was removed after the 2 hours and 100 µL MTT dissolved solution is again added. The plates were gently agitated until the formazan precipitate was dissolved; it was followed by measurement of OD value by spectrophotometer at 570nm and 690nm.

### 8.1 Cell Survival by MTT Assay results

**Cytotoxicity associated with curcumin distearate and dibutyl phthalate on Hela cells using a MTT assay. Cell Viability (%) with 0.125, 0.25, and 0.5 mg/mL of Curcumin distearate and DBP. Data are presented as mean±SE (n=4 replicates). Significant differences between plasticizers at different concentrations and control are indicated as ***p<<0.0001 (Student's t-test)**

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