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Contact Angle and Surface Tension of Some Solvents Used in Pharmaceuticals

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ABSTRACT

Many pharmaceutical dosage forms have been used the solvents in the production or related processes. These solvent characteristics have not been characterized such as contact angle and interfacial tension which should be considered for their applications. The aim of this study is to investigate the interfacial tension and contact angle of some solvents typically employed in pharmaceuticals. Interfacial tension (IFT) was determined using the drop shape analysis. The contact angle and contact angle with time measurements on the glass plate and PDMS surface were performed with the sessile drop technique on the goniometer. The viscosity of them was also determined. The nature properties of solvent such as interfacial tension and viscosity were the crucial characteristics affecting the contact angle and contact angle with time on the test materials. The volatile oil such as eucalyptus oil and peppermint oil could spread well on glass and PDMS. PEG and propylene glycol showed the medium IFT, rather low contact angle on glass but their contact angle on PDMS was rather high indicating their sharp hydrophilic characteristic. Silicone oil could spread well both on glass and PDMS. Almost of contact angle variations with time on glass exhibited the curve of contact angle with initial rapidly decreasing whereas the straight line with rather constant contact angle was evident on PDMS for most of test solvents. Therefore the obtained data related about IFT and contact angle of these test solvents should be beneficial for selecting the suitable solvents for the pharmaceutical applications.

**Keyword:** Solvent, pharmaceuticals, contact angle, surface tension

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INTRODUCTION

Many solvents have been used as vehicle, wetting agent and granulating fluid in pharmaceutical field. Many vegetable oils and some synthetic solvents (benzyl benzoate, peppermint oil and ethyl oleate) have been used as vehicle in oily injections [1]. Some liquids such as 2-pyrrolidone, tetra ethylene glycol, polyethylene glycol (PEG) and N-methyl pyrrolidone (NMP) have been claimed as biocompatible solvent for *in-situ* forming gel drug delivery system [2]. Glycerin, propylene glycol and PEG are mostly employed as co-solvent in liquid dosage forms and plasticizer for film coating. Triacetin and triethyl citrate are typically also used as plasticizer in film coating especially for ethyl cellulose or methacrylates film formers. Isopropyl myristate, NMP, propylene glycol and ethanol have been used as skin penetrating enhancer for transdermal drug delivery system.

The solvent basic properties such as contact angle and interfacial tension (IFT) should be considered for their applications. Typically, the wetting ability is described often by the value of a contact angle of a liquid on a solid surface. To determine the degree of wetting, the contact angle formed between the liquid and target solid surface is determined [3]. The smaller the contact angle and the surface tension, the greater the degree of wetting. After liquid drop is applied on the solid surface, a finite amount of time is required for the liquid to assume its equilibrium contact angle (θ).

$$\gamma_{sl}\cos\theta = \gamma_{sv}\text{-}\gamma_{sl}, \quad \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(1)$$

Where the variable γ refers to IFT of the solid-liquid (sl), solid-vapor (sv) and solid-liquid interfaces (sl). The electrolyte, surfactant or any solute could change the contact angle and surface free energy of the used liquids [4,5]

Polydimethylsiloxane (PDMS) has been most typically employed as standard polymeric film for contact angle measurement due to its low surface tension, hydrophobic property, stability against heat and oxidation, non-inflammability and non-toxicity [6]. The glass plate has been used as the hydrophilic solid surface. Materials with high surface energy such as glass plate exhibit an increase in the contact angles with the decrease in the surface tension of the spreading liquids.

The principle and knowledge of the surface tension and wetting behavior of solvent on the different target surfaces are crucial for basic physics and application such as cleaning, coating, printing, etc [7]. The data of surface energy and wettability has been employed in pharmaceutical field to indicate the interfacial interaction and compatibility among formula excipients. The predictive granule properties could be obtained from the binder-substrate spreading coefficient. The surface free energy (SFE) data based on solvent-drug spreading coefficients were the good indicator to apply for selection of the suitable granulating solvent for the wet granulation process [8]. For materials in field of tissue engineering, their surface

properties must be properly characterized and optimized since the surface topography could affect the cell adhesion and its growth behavior [9]. The hydrophilic and hydrophobic nature of the incorporated solvent as plasticizer should be considered for adjusting the prepared device for the properly desired characteristics. Therefore the aim of this study is to investigate the IFT and contact angle of some solvents typically employed in pharmaceuticals. The contact angle variation with time and viscosity of them was also determined.

MATERIALS AND METHODS

Materials

N-methyl-pyrrolidone (NMP) was purchased from Fluka, New Jersey, USA. Coconut oil which was the virgin coconut oil prepared by cold press was kindly provided from Tropicana Oil Co. Ltd., Nakhon Pathom, Thailand. Benzyl benzoate (Pharmaceutical Traders CO, LTD., Bangkok, Thailand), dicloromethane (244777-P, BrightchemSdnBhd, Pulau Pinang, Malaysia), ethanol (lot no. 617W62, J. T. Baker Solusorb, Malaysia), ethyl oleate (lot no. 1425705, Sigma-Aldrich Chemie GmbH, Buch, UK), olive oil (lot no. L9126R H1336, Sino-Pacific Trading Co, Ltd., Bangkok Thailand) and sesame oil (Namsiang Co., Ltd., Bangkok, Thailand) were used as received. Clove oil (Srichand United Dispensary Ltd. Partnership, Bangkok, Thailand), silicone oil (batch no. 1104551, Ajax Finechem Pty Ltd, NSW, Australia), triacetin (lot no. MKBG3776V, Sigma Aldrich, MO, USA), triethyl citrate (lot no. BCBBF0400, Sigma-Aldrich, MO, USA), 2-pyrrolidone (lot no. A0257476, Acros Organics, New Jersey, USA) and tetra ethylene glycol (batch no. 04322BJ, Aldrich, MO, USA) were used as received. Eugenol (batch no. DK8521), polyethylene glycol (PEG) 400 and 600 were purchased from PC Drug Center, Bangkok, Thailand. Isopropyl myristate, castor oil, eucalyptus oil, glycerin, propylene glycol, light mineral oil and peppermint oil were purchased from SR Lab Co., Bangkok, Thailand. Polydimethylsiloxane (PDMS) was prepared by mixing Sylgard®184 silicone elastomer base (lot n. 0006066761, Dow Chemical Corporation, MI, USA) and Sylgard®184 silicone elastomer curing agent (lot n. 0006066761, Dow Chemical Corporation, MI, USA) at the ratio of 10:1 at room temperature and coated on the glass plate by casting technique for 48 h before use.

Surface tension measurement

Interfacial tension (IFT) was determined using the drop shape analysis method on the goniometer (FTA 1000, First Ten Angstroms, USA) (pump out rate 2.5757 ul/s). From this method, surface tension was obtained by analyzing the change in the shape of a pendant drop of a liquid suspended in air. The surface tension of distilled water was also measured as the control (n=6).

Contact angle measurement

The wettability of different liquids were determined by contact angle measurement which was carried out by the liquid drop on the glass plate and PDMS surface using the drop

shape analysis (sessile drop technique) on the goniometer (FTA 1000, First Ten Angstroms, USA) with the pump out rate of 2.5757 ul/s at room temperature equipped with a CCD camera at 1st second of contact time frame grabber and image analysis software from First Ten Angstroms. The liquid was pumped out from the stainless tube and contacted onto the test solid surface and the recording of the contact angle was started when the liquid contacted with the glass or PDMS at 5 second (n=6). The contact angle variation with time for each solvent was also recorded by checking the change of contact angle during 0-15 sec or 0-25 sec.

Viscosity measurement

The solvents were determined their viscosity using Brookfield DV-III Ultra programmable rheometer (Brookfield Engineering Laboratories. Inc., USA) (n=3).

RESULTS AND DISCUSSION

The IFT and contact angle values on glass and PDMS of various solvents are summarized in Table 1. IFT of water was highest because of its hydrogen bonding whereas that of many oils such as isopropyl myristate and silicone oil was low due to their small force from hydrophobic bonding. This was indicative of the much weaker molecular interaction between molecules than that of water. This fact could be anticipated based simply on hydrogen bonding capability argument of water. Very low IFT of dichloromethane and ethanol was evident indicating the low molecular interaction therefore these liquid were easy to evaporate. In addition, their wetting on glass plate was good since they could notably spread on the glass. Additionally, the liquids with low surface tension could improve the wettability of the substrates causing an increase in wetted drop base area accompanied by a decrease in the drop height. This low contact angle on glass plate did not owing to their evaporation of these two solvents since there was the remaining of them during the time interval of this study and rather constant contact angle were apparently evident on PDMS. When the liquid possesses a high vapor pressure, its sessile drop contact angle experiment in open system should be considered which several reports concluded that such a situation the accurate result could not be obtained [10-12]. The presence of a curved liquid-vapor interface involved that the vapor pressure in equilibrium with the liquid drop was higher than the vapor liquid in equilibrium with the same liquid in unlimited phase. Therefore a measure of contact angle in perfect thermodynamic equilibrium should be performed in a closed container where the sessile drop of liquid was in the presence of its own atmosphere [13].

From this study, we found that the contact angle of some oils such as isopropyl myristate, silicone oil, olive oil and coconut oil was rather low on glass plate (Table 1). Especially, the volatile oil such as peppermint oil and eucalyptus oil exhibited the very low contact angle on glass therefore the component of them which were hydrophilic might spread well on the glass. PEG and propylene glycol showed the medium IFT, rather low contact angle on glass but their contact angle on PDMS was rather high indicating their sharp hydrophilic characteristic. Although the chemical composition of glycerin is hydrophilic it showed rather

high contact angle on glass and also apparently high on PDMS. This result was corresponding with its unique high viscosity as presented in Table 1 that might retard its spreading and wetting. This observation was also found in the case of castor oil. Therefore the contact angles depended on the viscosity of the liquids. Higher viscosity liquids tended to produce the low wettability caused by higher viscous dissipation that reduced the spreading rate. This coincided with a decrease in the wetted drop base area and an increase in the drop height. However the high viscous oil such as silicone oil its contact angle on glass and PDMS were ostensibly low which indicated its property for good spreading. Liquids with lower surface tension prevailed the better wettability and vice versa. The low contact angle indicated that the droplet of that solvent spread over and wet the surface immediately after they were deposited on the surface. This result was evident for the alcohol on the hydrophilic PDMS with modified by fluorination [6]. Therefore the contact angle of the low viscous oils (eucalyptus oil and isopropyl myristate) was also low on glass and rather low on PDMS.

Table I: Interfacial tension (IFT), contact angle (CA)on glass and PDMS film and viscosity with 100 rpm; shear rate of 750 sec^{-1} of different solvents.

Solvent	IFT (N/m)	Contact angle on glass($^{\circ}$)	Contact angle on PDMS ($^{\circ}$)	Viscosity (cps)
2-Pyrollidone	47.36±0.31	23.49±10.60	75.78±0.40	22.54±0.37
Benzyl benzoate	32.33±0.31	30.56±8.03	78.08±0.85	9.05±0.03
Castor oil	40.68±2.25	48.19±2.46	74.59±1.18	474.10±33.41
Clove oil	28.12±1.33	12.74±3.83	62.42±3.32	17.25±0.67
Coconut oil	28.22±0.59	22.42±4.27	53.99±5.23	51.70±1.07
Dichloromethane(DCM)	20.20±0.34	3.66±2.48	39.98±1.14	ND
Ethanol(EtOH)	28.98±1.29	7.70±6.74	29.31±0.65	1.31±0.10**
Ethyl oleate	34.08±0.15	12.60±0.78	42.22±1.38	6.61±0.30
Eucalyptus oil	34.57±0.38	4.39±1.46	44.34±0.29	5.37±0.86
Eugenol	24.03±0.90	24.93±2.96	68.74±1.50	11.03±0.66
Glycerin	46.88±2.84	53.36±2.92	92.94±0.70	688.90±15.07*
Isopropyl myristate	28.59±0.34	9.50±1.62	38.45±0.97	5.63±0.12
Light mineral oil(LMO)	30.63±0.96	23.52±1.34	57.75±1.07	34.01±1.07**
N-methyl pyrrolidone (NMP)	45.69±0.11	16.19±3.44	70.37±2.71	2.38±0.38
Olive oil	27.22±2.68	22.38±2.34	47.06±5.20	74.99±0.38**
Peppermint oil	35.89±0.36	7.71±0.40	49.13±0.87	10.64±0.44
Polyethylene glycol(PEG) 400	38.20±0.25	41.89±1.37	91.67±1.51	74.77±1.36
Polyethylene glycol(PEG) 600	40.57±0.49	28.35±2.17	89.05±3.01	100.91±2.29**
Propylene glycol(PG)	41.38±0.72	25.22±1.13	74.07±7.94	43.46±1.61
Sesame oil	30.29±0.45	28.13±2.28	69.40±1.81	64.34±1.69
Silicone oil	24.07±0.10	22.03±0.59	26.44±1.71	361.00±3.44***
Tetra ethylene glycol	58.28±0.12	39.61±0.84	92.76±1.09	35.32±0.66
Triacetin	35.79±0.06	40.58±5.69	77.96±4.29	14.78±1.20
Triethyl citrate	33.70±0.09	34.68±4.15	72.59±0.82	27.51±0.30
Water	74.52±0.21	26.60±2.83	99.09±2.85	1.34±0.32**

*10 rpm; shear rate of 8 sec^{-1}, **10 rpm; shear rate of 75 sec^{-1}, ***5 rpm; shear rate of 38 sec^{-1}

By comparison, most of the contact angle variation with time obtained on glass exhibited the curve of contact angle decreasing as seen in Table 2 (left) whereas the straight line with rather constant contact angle on PDMS was seen for most solvents (Fig. 1). The rapid decrease was evident in the initial phase of contact angle variation with time plot. However this observation was not found for water both on glass and PDMS. Therefore the high IFT of water indicating its high cohesive force and that it could retain effectively its shape on solid material whereas the initial contact of other solvents on solid material could gradually change its equilibrium for adjusting its shape to minimize their free energy. The finite amount of time was required for the liquid to assume its equilibrium contact angle after liquid drop was applied on the target solid surface. For low viscosity liquid, the relaxation of contact angle from initial (high) value to an equilibrium (low) value can take seconds [3]. The very fast decrease of contact angle of dichloromethane and eucalyptus oil on glass was seen while it was apparently stable on PDMS. The noticeable decrease of contact angle on PDMS was found for ethyl oleate, peppermint oil and especially silicone oil. The decrease in the initial contact angle for liquids of lower surface tension was sharper than that of liquid of high surface tension reflecting that wetting with the latter group was not spontaneous as compared to wetting with the first group. This observation emphasized on the role of interfacial tension in affecting wettability. Therefore, the addition of surfactants becomes a common practice to enhance the spreading and wettability by reducing surface tension of the fluids [13]. The photographs exhibited the contact angle on glass and PDMS of some solvents (tetra ethylene glycol, sesame oil and eucalyptus oil) are presented in Fig. 2. The apparent low contact angle of eucalyptus oil was seen both on glass and PDMS. For tetra ethylene glycol which is the hydrophilic substance its contact angle on PDMS was higher than that on the glass plate.

Table 2: Dielectric constant, boiling point and density of some solvents from other literatures

Solvent	Dielectric constant	Boiling point (°C)	Density (g/ml)	Viscosity (cps)	Surface tension(N/m)
Castor oil	4.478		0.9612		
Coconut oil	3.254		0.9204		
Dichloromethane	9.1	40	1.3266	0.41	27.8
Ethanol	24.55	79	0.7890	1.07	22.0
Glycerin	43.5		1.2610	934	76.2 or 63
PEG 400	12.4				
Propylene glycol	32.1				
NMP			1.025	1.67	44.6
Olive oil	3.252		0.9125		
Sasame oil	3.365		0.9132		
Water	80.4	100	1.0000	0.89	72.7

*Dielectric constant of PDMS is 2.3-2.8

Table 2 shows some properties (dielectric constant, boiling point, density, viscosity and surface tension) of some solvents collected from the other literatures. Dielectric constant can be determined by oscillometry, in which the frequency of a signal is kept constant by electrically changing the capacitance between the two parallel plates. Generally, the dielectric constant provides the rough measure of the solvent polarity which this value indicates the

ability of solvent to reduce the strength of the electric field surrounding a charged particle immersed in it which this reduction is then compared to the field strength of the charged particle in vacuum. Practically, the solvents with a dielectric constant of less than 15 are generally classified to be nonpolar. Therefore this study was also included this property from the literature for data analysis. The low dielectric constant of PDMS clearly indicated its hydrophobic surface (Table 2). However the low dielectric constant of oils indicating their hydrophobicity did not correspond well with our results as previously described. The selected vegetable oils studied here provide a fairly complete range, castor oil containing hydroxyl and hydroxyesters, olive oil and sesame oil containing the unsaturated ones and the coconut oil contained the completely saturated ester. The values for the electric moments of these oil molecules therefore supported the reasonably moments of vegetable oils that their dielectric constant values were in the range 2.7-3.7 depending on the constitution of the acids of which they were composed [14,15]. The solvent with higher vapor pressure owing to its low boiling point exhibited the low contact angle on both glass and PDMS which indicated their good spreading on these solid substrates. The obtained IFT of glycerin from this experiment was lower than that from the literature whereas that of the others was similar to the value from the literature. However the relationship between density and contact angle was rather difficult to predict [16].
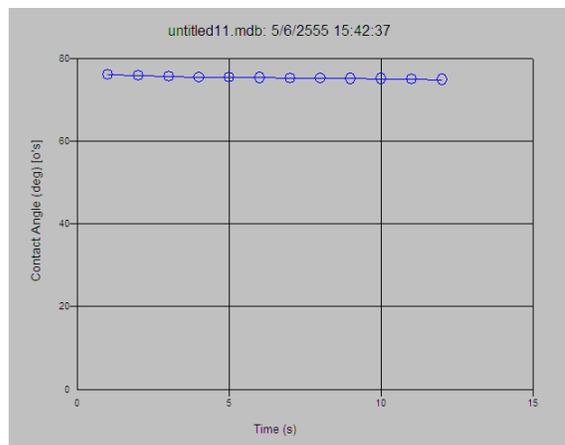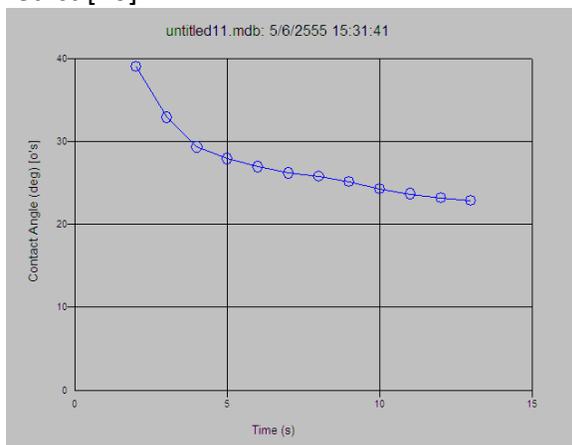
2-Pyrollidone
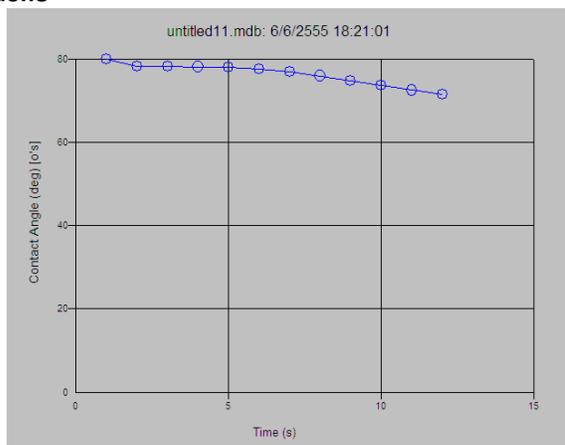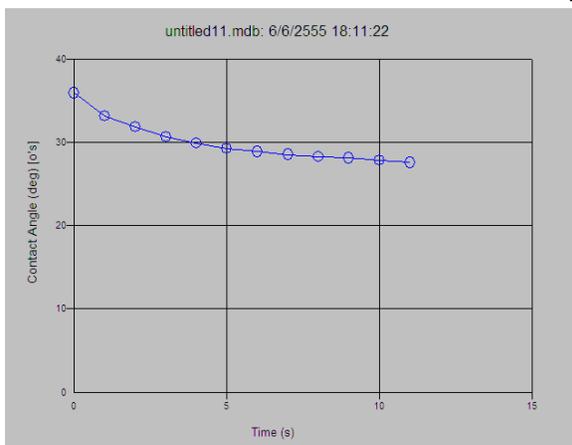
Benzyl benzoate
Fig. 1 Contact angle variation with time of different solvents (left: on glass and right: on PDMS)
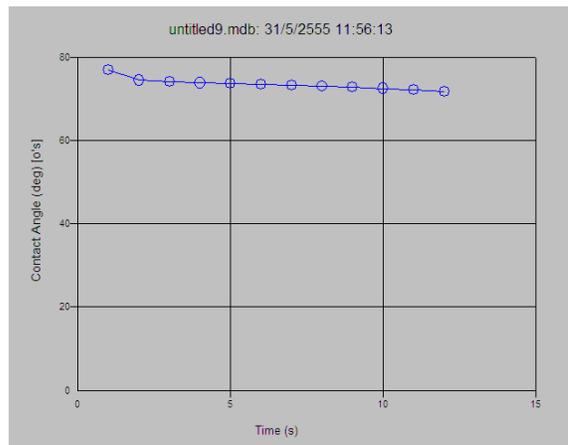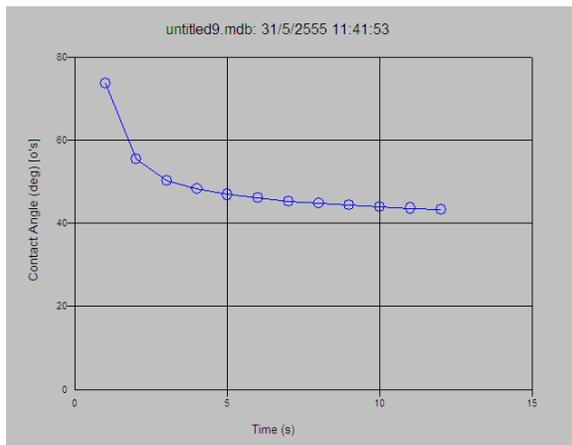
Castor oil
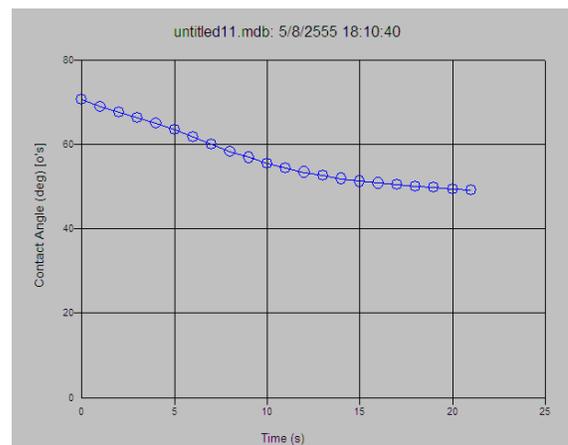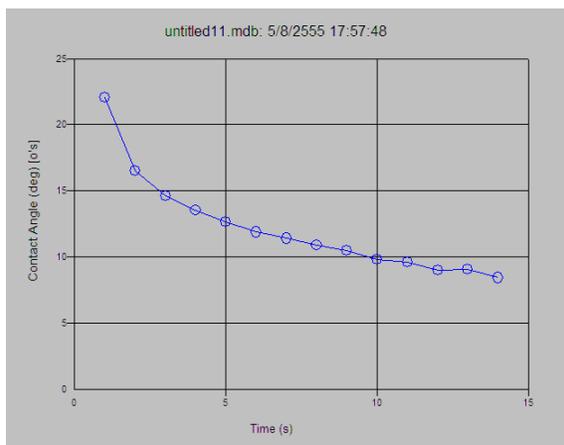
Clove oil
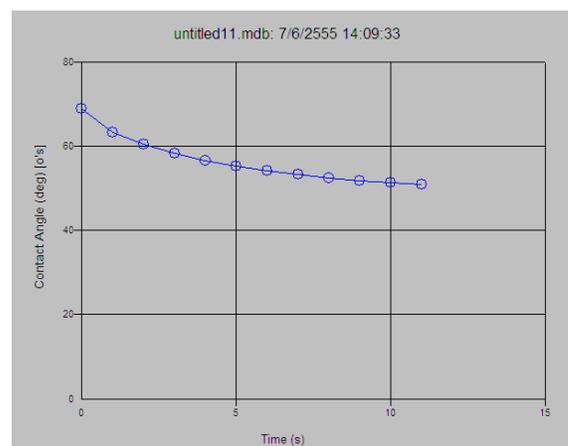
Coconut oil

Fig. 1 Contact angle variation with time of different solvents (left: on glass and right: on PDMS)
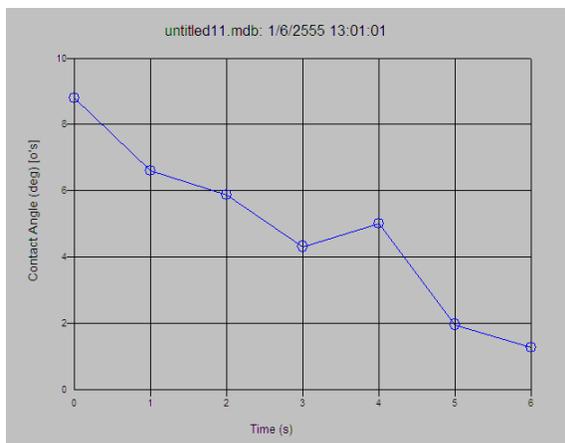
Dichloromethane
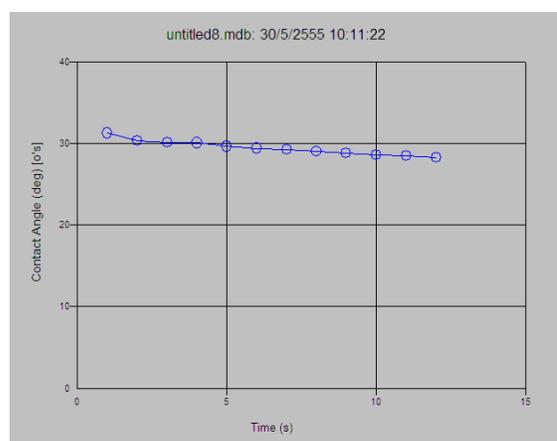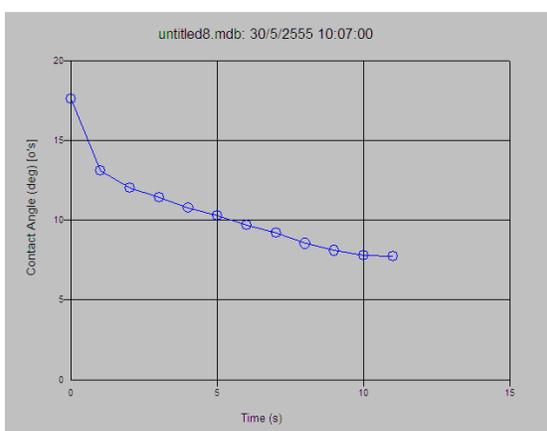

Ethanol
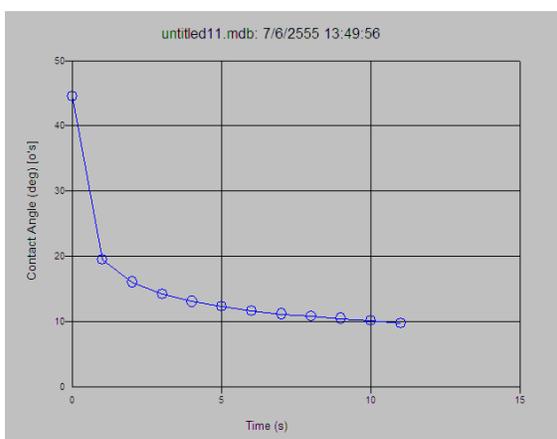
Ethyl oleate

Fig. 1   Contact angle variation with time of different solvents(left: on glass and right: on PDMS) (continued)
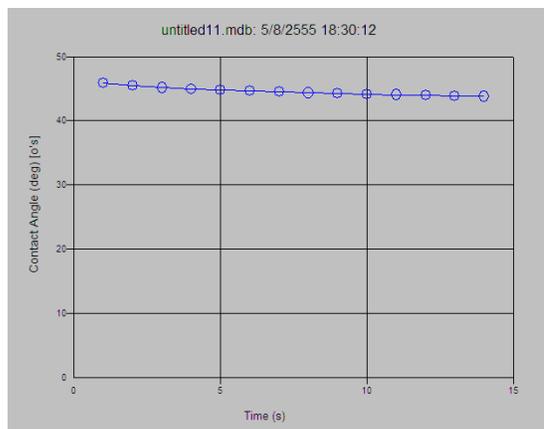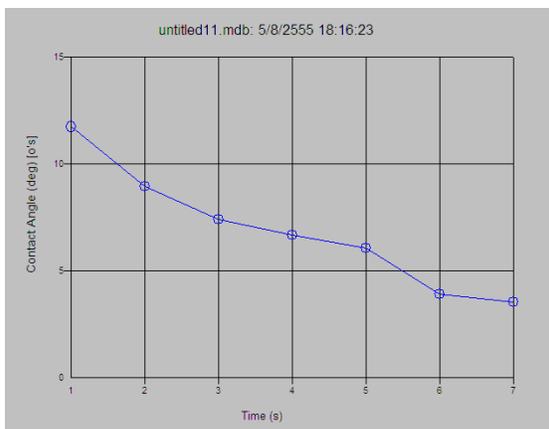
Eucalyptus oil
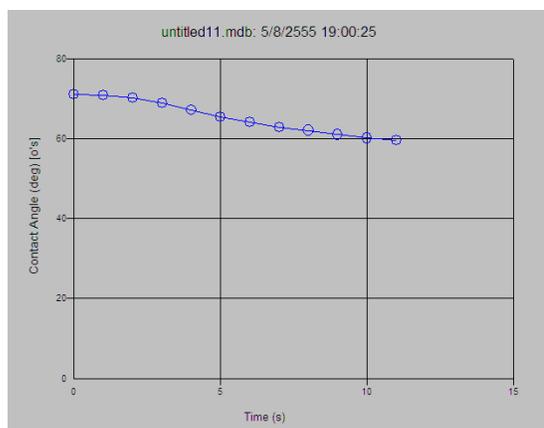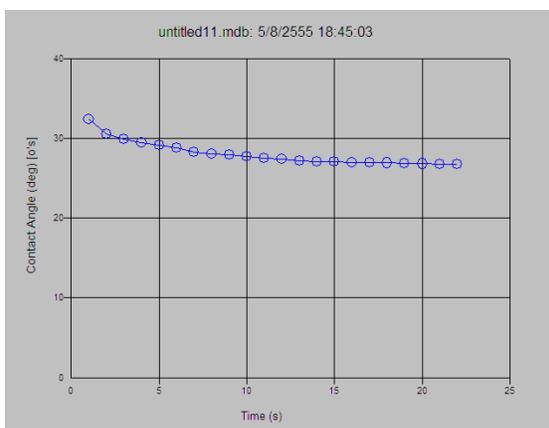
Eugenol
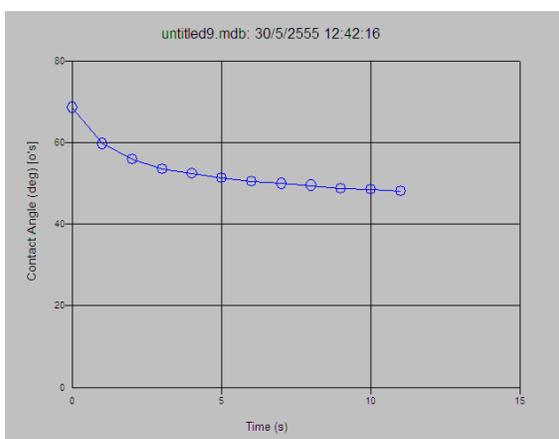
Glycerin

Fig. 1 Contact angle variation with time of different solvents (left: on glass and right: on PDMS)(continued)
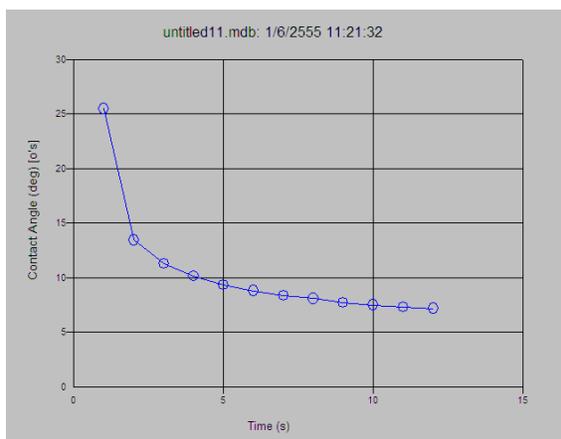
Isopropyl myristate
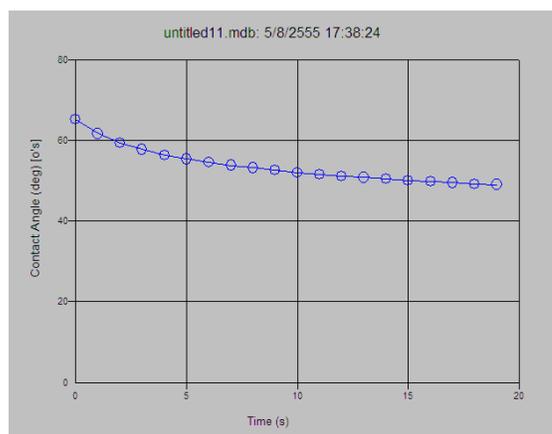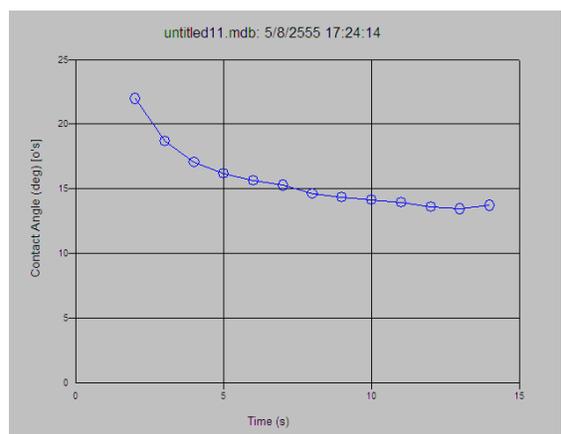
Light mineral oil
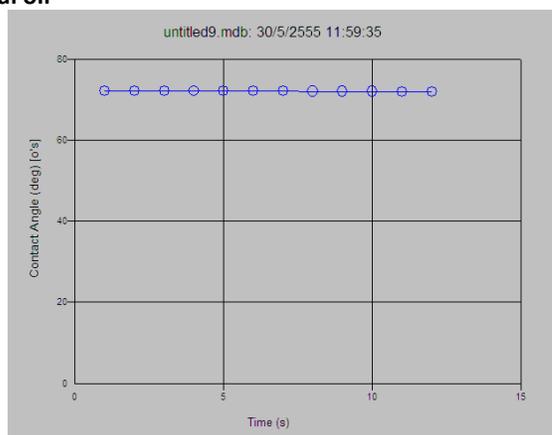
NMP

Fig. 1   Contact angle variation with time of different solvents(left: on glass and right: on PDMS)(continued)
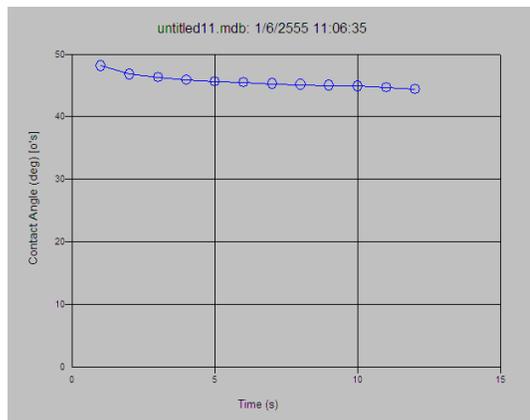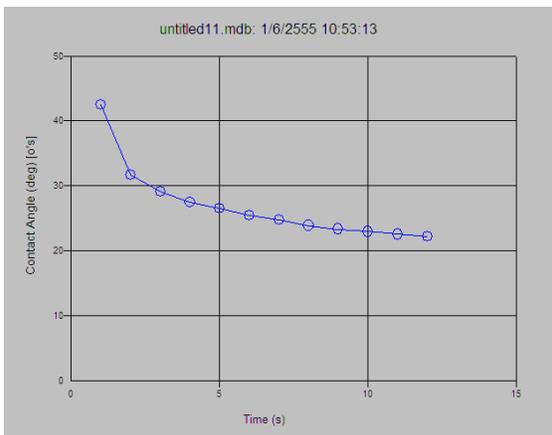
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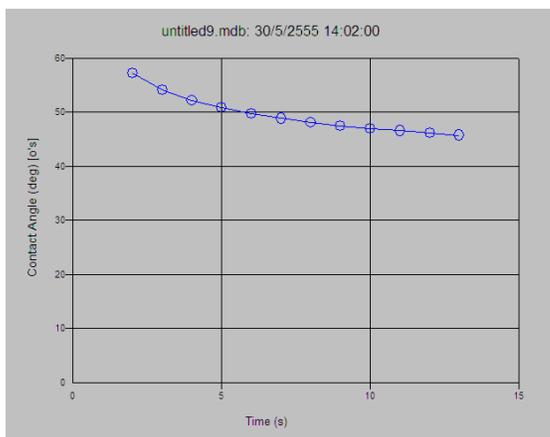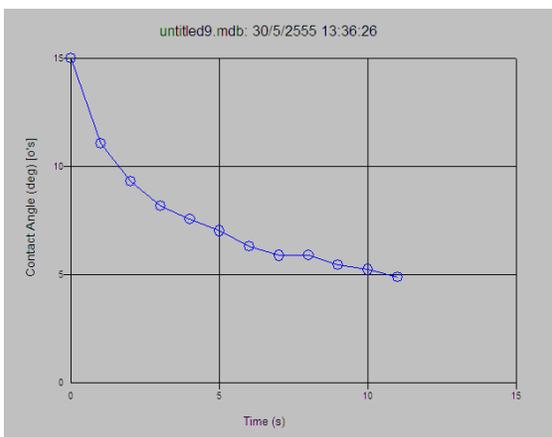
Peppermint oil
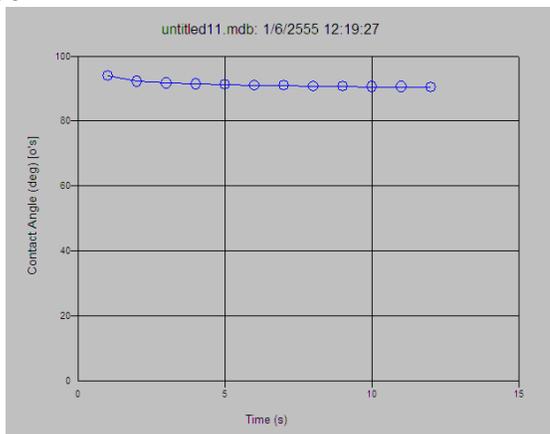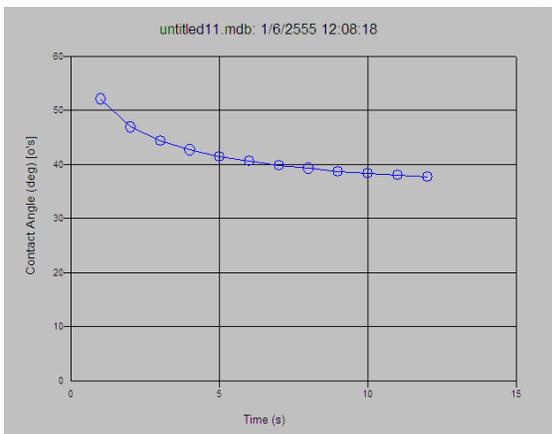
Polyethylene glycol(PEG) 400

Fig. 1   Contact angle variation with time of different solvents(left: on glass and right: on PDMS) (continued)
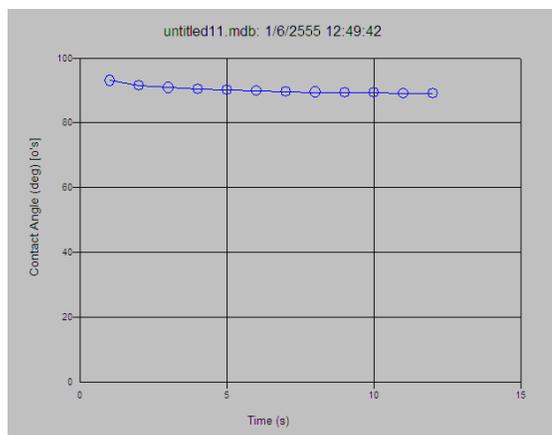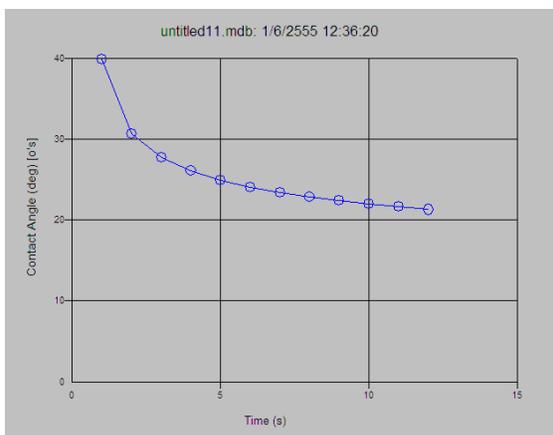
Polyethylene glycol(PEG) 600
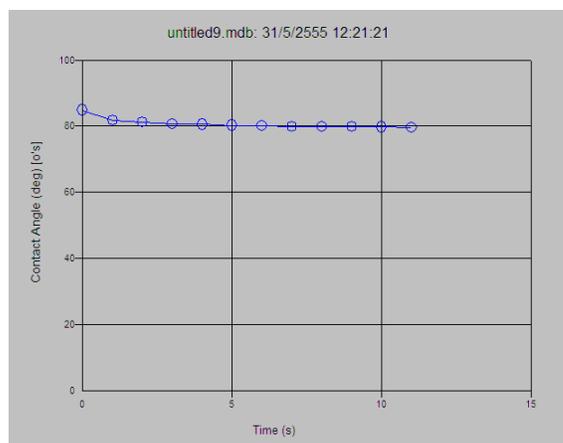
Propylene glycol(PG)
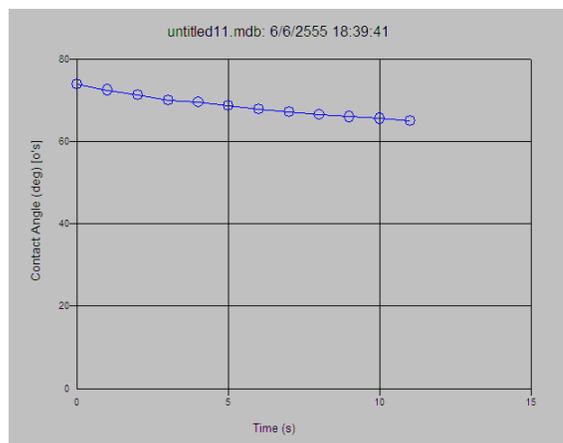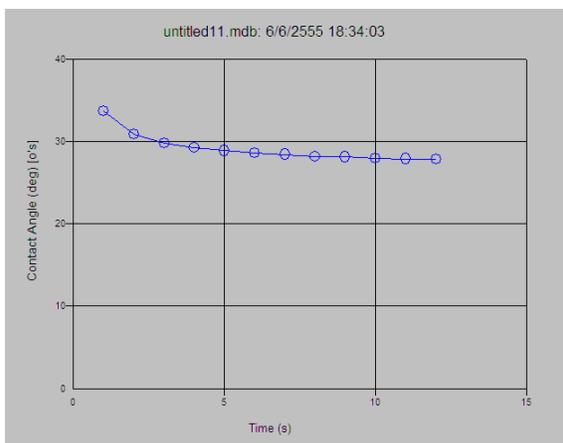
Sesame oil

Fig. 1   Contact angle variation with time of different solvents(left: on glass and right: on PDMS)(continued)
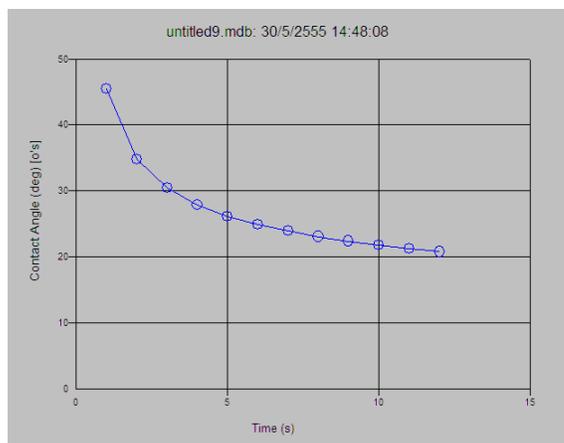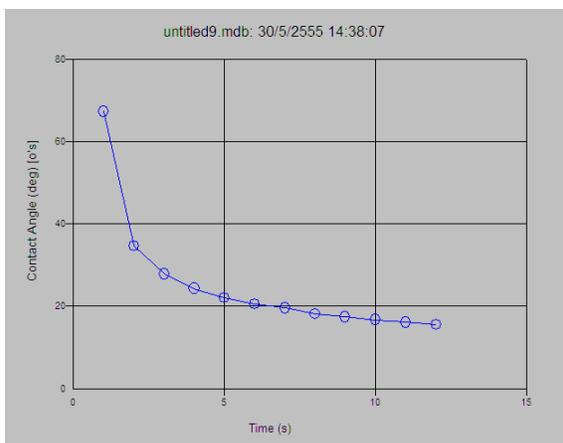
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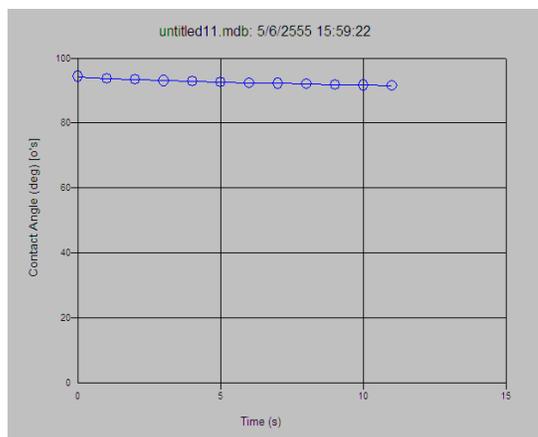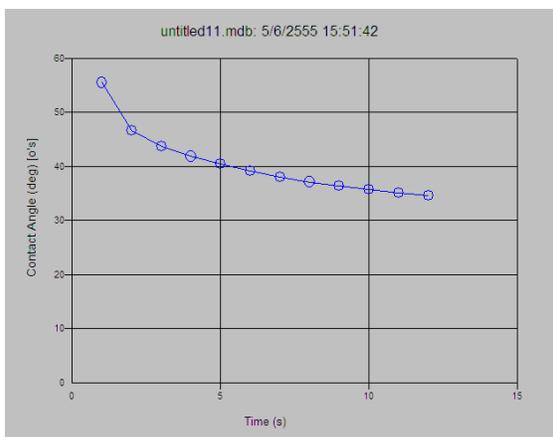
Tetra ethylene glycol
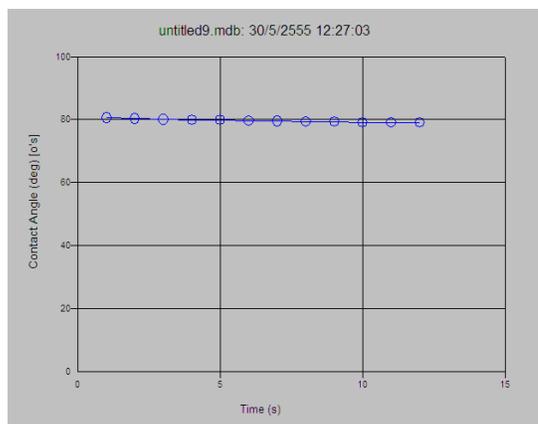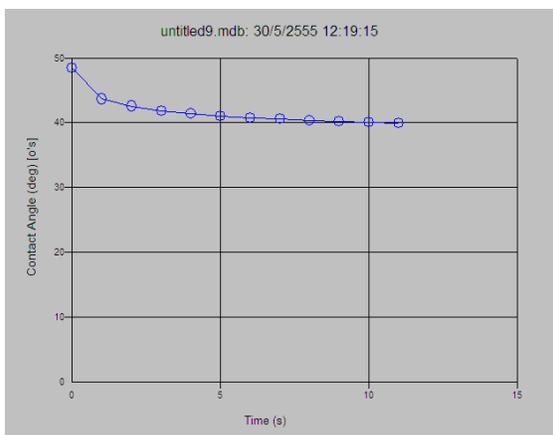
Triacetin

Fig. 1   Contact angle variation with time of different solvents(left: on glass and right: on PDMS)(continued)
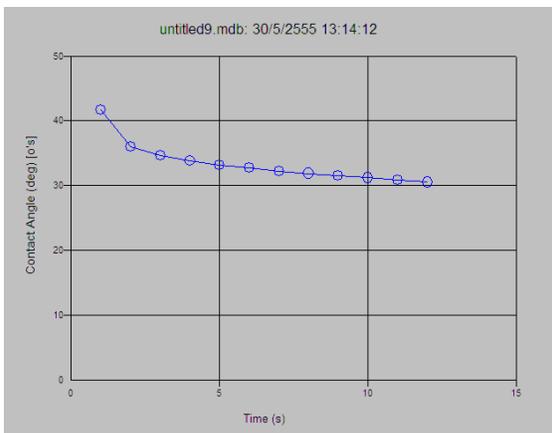
Triethyl citrate
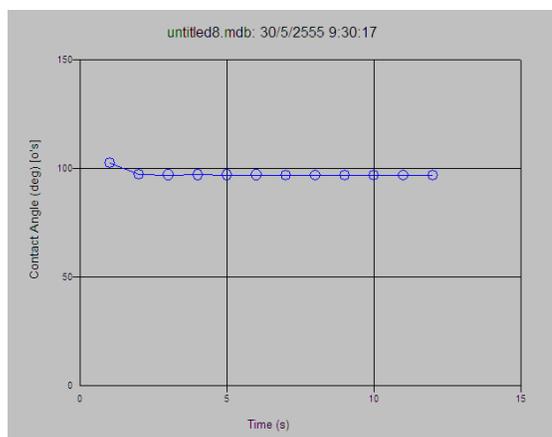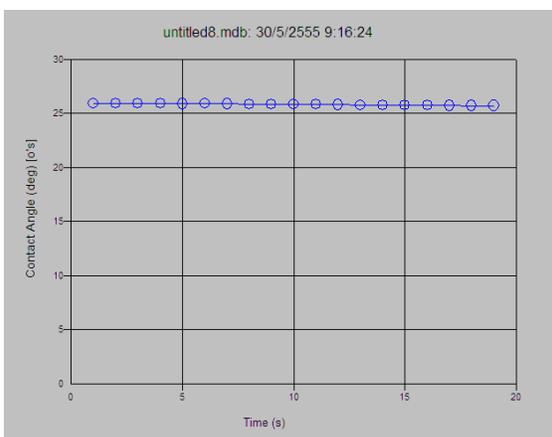
Water
Fig 1: Contact angle variation with time of different solvents(left: on glass and right: on PDMS)(continued)
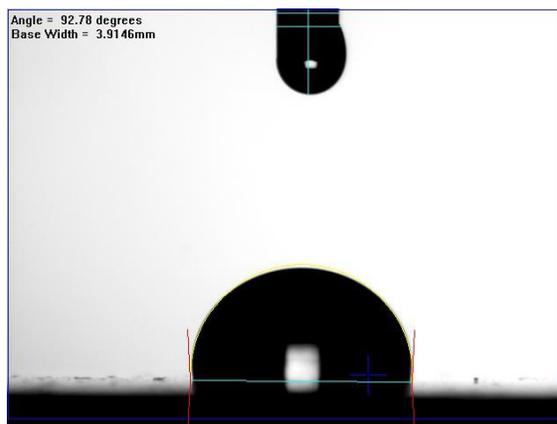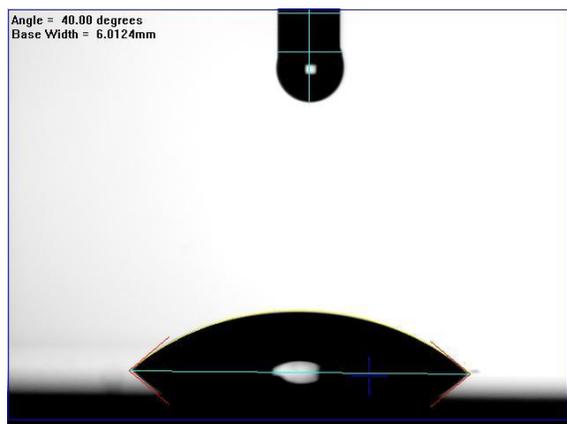
Tetra ethylene glycol

Fig 2: Contact angle of different solvents (left: on glass and right: on PDMS)

Sesame oil

Eucalyptus oil
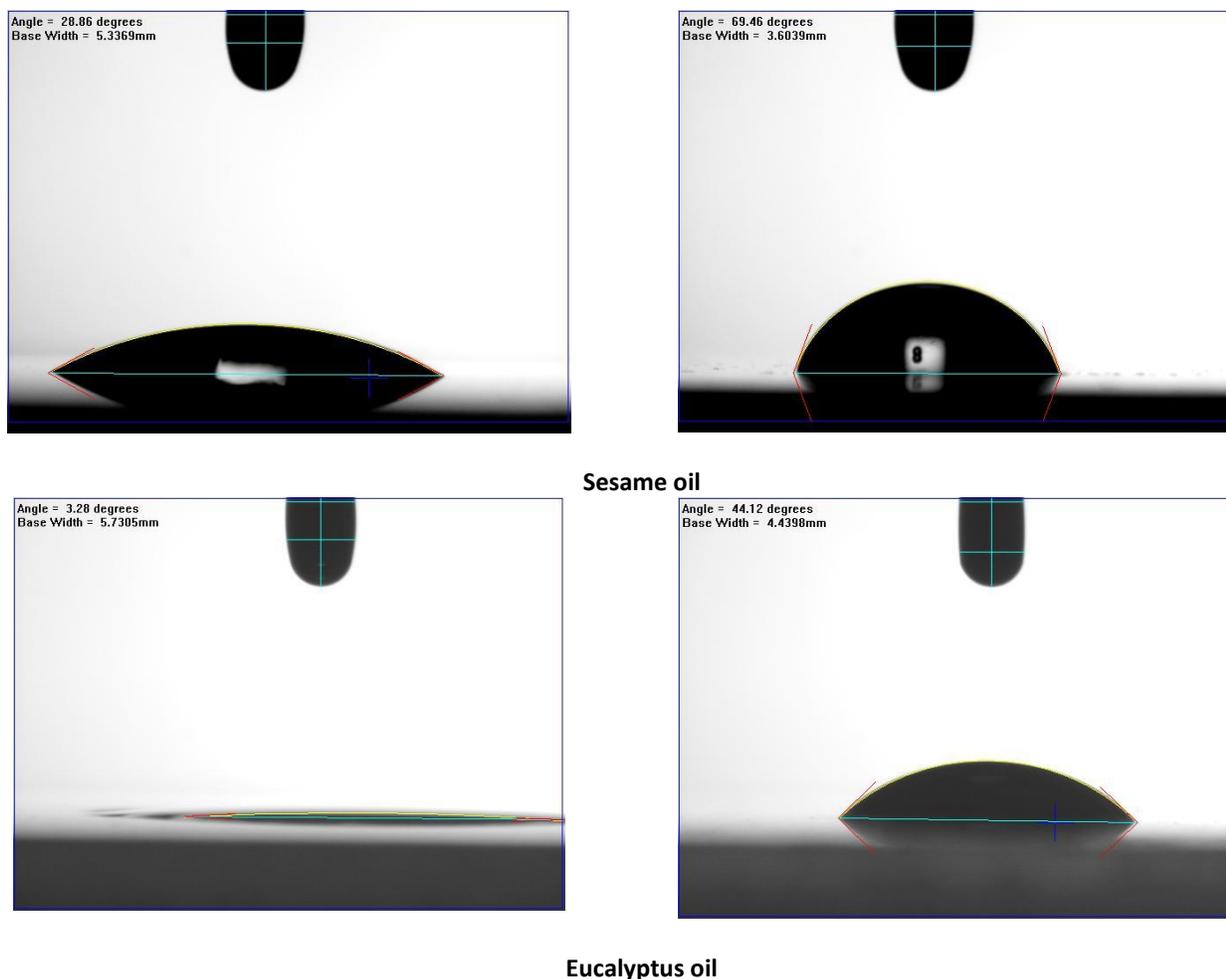
Fig 2: Contact angle of different solvents (left: on glass and right: on PDMS) (continued)

CONCLUSION

The various solvents used in field of pharmaceuticals were tested for their surface tension and contact angle on glass and PDMS. The nature properties of solvent such as interfacial tension and viscosity were the crucial characteristics affecting the contact angle and contact angle with time on the test materials.

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