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Studies on physical /chemical compatibility between synthetic and herbal drugs with various pharmaceutical excipients

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ABSTRACT

Stability of Pharmaceutical formulations are oftenly challenged by compatibility between drugs and excipients. The objective of the present study is to identify compatibility between drug:drug and drugs:excipient. Curcumin and Tretinoin were selected as model drug where Ethyl cellulose (EC) and Poly vinyl alcohol (PVA) as excipients. The study was done by Fourier transform infrared spectroscopy (FTIR), X-ray diffraction study (XRD) and Thin layer chromatography (TLC). The spectrophotometric graphs revealed that there was no significant changes in position of functional groups of Curcumin, Tretinoin, EC and PVA (O-H, C=O, C-H str.) in pure drugs and excipients with respect to their physical mixtures. X-ray diffraction study reflects that the characteristic peaks of curcumin appeared at a diffraction angle of 2□ at 7.95^0, 8.80^0, 12.28^0, 17.29^0 showing that Curcumin and Tretinoin was present as a crystalline form as well. The R_f values of the physical mixtures obtained from TLC study on the 0^{th} and 30^{th} day were approximately similar to the R_f values of the pure Curcumin and Tretinoin. The above spectrophotometric data and retention factor clearly implies that the synthetic-herbal drug combinations with pharmaceutical excipients are compatible with each other and can be introduced for successful development of novel drug delivery system.

Keywords: FTIR, Compatibility study, TLC, Curcumin, Tretinoin, XRD.

INTRODUCTION

Assessment of drug-drug-excipients compatibility is very important to identify product's stability as well as its reproducibility with ensured therapeutic efficacy[1]. Although excipients selected for pharmaceutical formulations bears no pharmacological significance i.e. inert in nature[2]. But the excipients may participate in physical and chemical interaction and cause serious degradation of active pharmaceutical ingredients with poor dissolution rate and non-

uniformity of dose[3]. Over the decade, various methods have been developed to identify drug-excipients compatibility. It's very essential to conduct such studies as a part of formulation development process[4]. A number of multifactorial diseases like Acne, Psoriasis etc. needs two or more drug combination for effective treatment[5,6] The definition of combination products are clearly mentioned by Food and Drug Administration under section 21 CFR 3.2 (e). Multi drug combination came into light with respect to the patient compliance as well[7,8] The functional groups within the drug molecule may change the activity of each other, hence alters the therapeutic affectivity[9].EC is cellulose derivative where some of the hydroxyl groups on the repeating glucose units are converted into ethyl ether group and is a choice of pharmaceutical manufacturer due to its good film forming properties[10]. PVA is a excellent film forming and adhesive properties and prepared by partial or complete hydrolysis of polyvinyl acetate[11]. Various analytical tools viz. FTIR, XRD, SEM, separation technique viz. TLC etc. provides data indicating alteration in position of functional groups of drug in physical mixtures[12,13,14].

MATERIALS AND METHODS

Fourier transform infrared spectrophotometry study was done with Shimadzu Model (30.000:1), model no. 3116465 with wave no. range 7800 to 350 cm^{-1}, peak-to-peak, 4 cm^{-1} resolution, in a neighborhood of 2,100 cm^{-1}, 1-minute accumulation and having resolution of 0.5, 1, 2, 4, 8, or 16 cm^{-1}. X-Ray diffraction study of drug combination was identified by model XRD-6000, having the selectivity of independent dual axis θ-2θ linkage drive, independent 2θ axis and θ axis drives.Tretinoin is obtained from Shalaks Pharmaceuticals Private Limited, New Delhi and Curcumin is gift sample obtained from RYM Exporters, New Delhi.

FT-IR studies

Sample/KBr ratio

The concentration of the sample in KBr should be in the range of 0.2% to 1%. The pellet is much thicker than a liquid film, hence a lower concentration in the sample is required (Beer's Law). Too high a concentration usually causes difficulties obtaining clear pellets. The IR beam is absorbed completely, or scattered from the sample which results in very noisy spectra[15].

Sample preparation

Completely dried potassium bromide was transferred into a mortar. About 2 % of drug sample was weighed in digital balance, mixed and grind to a fine powder. Two stainless steel disks were taken out of the desiccator. A piece of the precut cardboard (in the tin can next to the oven) on top of one disk was placed and cutout hole was filled with the finely ground mixture. The second stainless steel disk was kept on top and transfers the sandwich onto the pistil in the hydraulic press. With a pumping movement, hydraulic pump handle moved downward. The pistil will start to move upward until it reaches the top of the pump chamber. Then, the pump handle moved upwards and continued pumping until the pressure reaches 20,000 prf. Rest for a few seconds and with the small lever on the left side, the pressure was released. Removing of the disks and pulling apart. Obtained film was homogenous and transparent in appearance. Than inserted into the IR sample holder and attach with scotch tape and run the spectrum[16].

The physical mixtures of drugs were prepared in 1:1 ratio and then passed through sieve # 30. Samples of drug and excipients were placed in vial, closed and labelled. Then the vials were

stored under two different conditions at 4˚C and at 40˚C±75% RH. Observations of all the mixtures were done on 0^{th} day, 7^{th} day, 15^{th} day and 30^{th} day. The compatibility of drugs with excipients was studied by FT-IR.

X-Ray Diffractometry

The solid state of the drugs was investigated by X-ray powder difractometry with Bragg-Brentano geometry at a wavelength of 1.5406. Powder X-ray difractograms were recorded in a diffraction angle (2θ) range of 2^0-40^0 using a step size of 0.03^0 under an exposure time of 8s[17,18].

Thin Layer Chromatography

The specified amount of drug and cream bases were weighed separately and mixed properly with the help of spatula. Mixture of drug and cream bases was placed in vial, closed and labelled. Then the vials were stored under two different conditions at 4˚C and at 40˚C±75% RH. Observations of all the mixtures were done on 0^{th} day, 7^{th} day, 15^{th} day and 30^{th} day. The compatibility of drugs with oily bases was studied by thin layer chromatography[19,20].

RESULTS AND DISCUSSION

Data obtained from FT-IR spectrophotometric study clearly indicates insignificant changes in spectra obtained from physical mixture of drugs and excipients. Spectra obtained from pure Curcumin were found 1759.41 cm^{-1} and 3491 cm^{-1} for C=O and O-H str.(Figure 1) respectively and in case of Tretinoin it was observed 1685.87 cm^{-1} and 2937.68 cm^{-1} (Figure 2) respectively. FT-IR spectroscopy of drugs shows very close spectra of the pure component 1758.23cm^{-1} and 1672.24 cm^{-1} for C=O str.; 3517.78 $cm^{-1}$and 2933.87 cm^{-1} for O-H str. (Figure 3) Spectrograph of both the drugs and excipients physical mixture shows 3517.78 cm^{-1}, 2933.87 cm^{-1}, 3415.69 cm^{-1} and 3346.43cm^{-1} for O-H str. group.

Spectrography of C=O str. shows sharp peak at 1758.23 cm^{-1}, 1672.24 cm^{-1} for Curcumin and Tretinoin respectively. C-H str. group for EC and PVA indicates sharp peak at 2868.55 cm^{-1} and 2909.12 cm^{-1} (Figure 4) respectively. Which indicates no interference between them (Table 2). There was no major changes in peaks of ketone (C=O), Hydroxyl (O-H) and methyl (C-H), in reference to the observed value of Curcumin and Tretinoin (Figure 1).

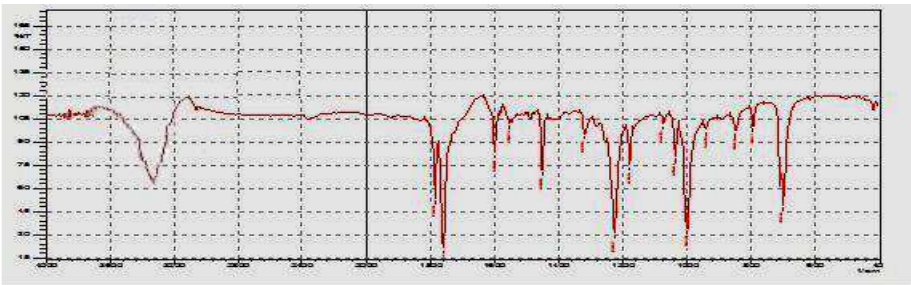

Figure 1: FT-IR interpretation of Curcumin

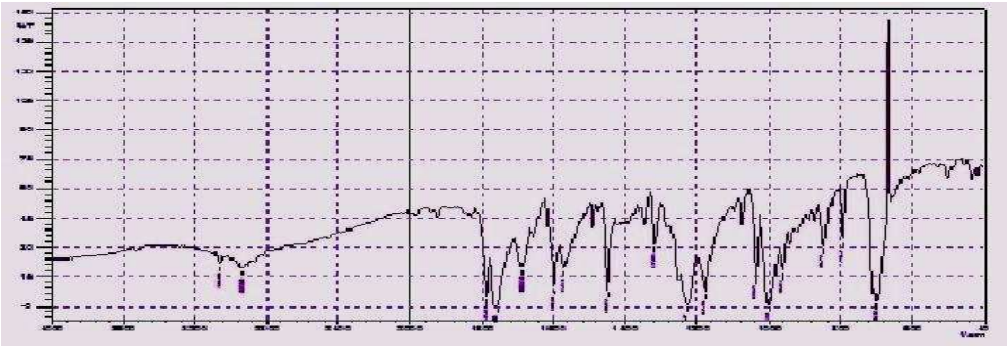

Figure 2: FT-IR interpretation of Tretinoin

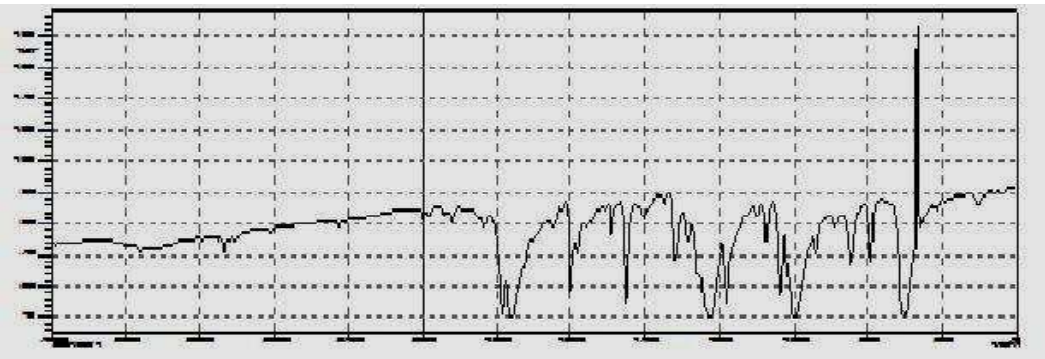

Figure 3: FT-IR spectra of Curcumin and Tretinoin combination

Table 1: FT-IR spectra of Curcumin and Tretinoin combination

S. No.	Functional Gr.	Wave length (cm^{-1})				
		Standard Absobance	Curcumin		Tretinoin	
			Pure drug	PM	Pure drug	PM
1	O-H str.	2700- 3800	3491.72	3507.41	2937.68	2925.22
2	C=O str.	1650-1780	1759.41	1768.11	1685.87	1692.86

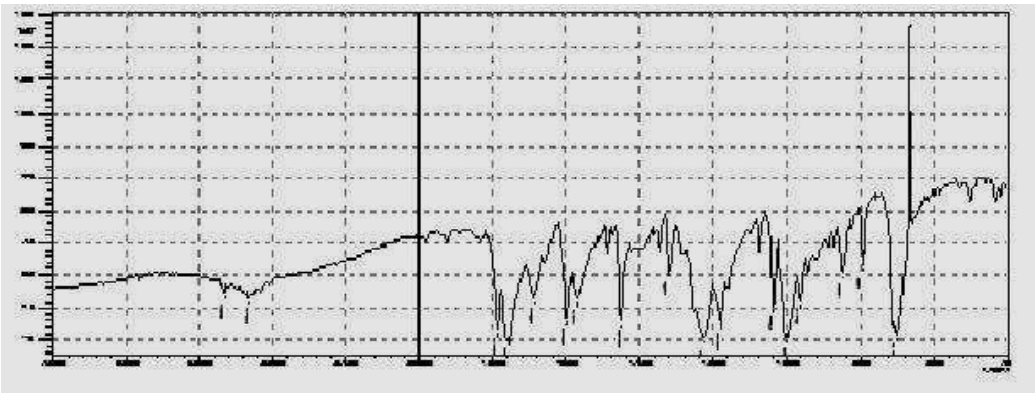

Figure 4: FT-IR spectra of Curcumin+ Tretinoin + PVA+EC

Table 2: FT-IR spectroscopy data of Drugs and excipients

S. no	F.G.	Curcumin+Tretinoin			Curcumin+Tretinoin+PVA				Curcumin+Tretinoin+PVA+EC				
		Standard (cm^{-1})	Curcumin (cm^{-1})	Tretinoin (cm^{-1})	Standard (cm^{-1})	Curcumin (cm^{-1})	Tretinoin (cm^{-1})	PVA (cm^{-1})	Standard (cm^{-1})	Curcumin (cm^{-1})	Tretinoin (cm^{-1})	PVA (cm^{-1})	EC (cm^{-1})
1	**O-H**	2700-3800	3507.41	2925.22	2700- 3800	3529.34	2947.19	3435.43	2700- 3800	3517.78	2933.87	3415.69	3346.43
2	**C=O**	1650-1780	1768.11	1692.86	1650-1780	1749.56	1703.37	NA	1650-1780	1758.23	1672.24	NA	NA
3	**C-H**	2700-3800	NA	NA	2700- 3800	NA	NA	2859.87	2700- 3800	NA	NA	2868.55	2909.12

F.G.: Functional Group

The powder X-ray diffractograms of pure Curcumin and Tretinoin reveals that characteristic peaks of curcumin appeared at a diffraction angle of 2□ at 7.95, 8.80, 12.28, 17.29^0 showing Curcumin was present as a crystalline form. The diffraction patterns of physical mixtures showed several peaks which is similar to that in pure form, indicating that the crystallinity of curcumin and tretinoin was not changed (Figure 5).

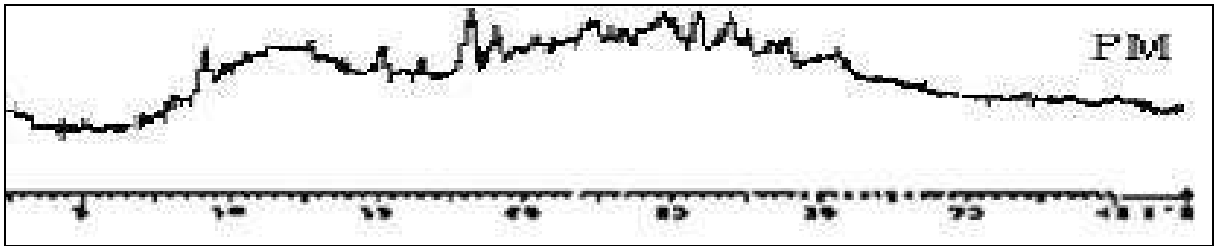

Figure 5: Powder X-ray diffraction of pure Tretinoin and Curcumin physical mixture

TLC studies showed that the R_f values of the mixture obtained on the 0th and 30th day were approximately similar to the R_f values of the pure Tretinoin and Curcumin. Therefore, it was concluded that both the drugs were compatible with each other (Table 3).

Table 3: Compatibility study of Tretinoin and Curcumin by TLC method

S. No.	Drug	R_f values			
		0th day		30th day	
		4 ^{0}C	45^{0}C/75% RH	4 ^{0}C	45^{0}C/75% RH
1	Tretinoin	0.959	0.957	0.977	0.974
2	Curcumin	0.776	0.774	0.773	0.778

CONCLUSION

The data obtained from FT-IR spectroscopy, X-Ray diffraction and TLC study clearly indicates no interaction between drug and excipients, hence synthetic and herbal drug combination is safe to formulate in a novel dosage form. To identify drug release pattern from novel delivery system, we will go for cream formulation in future.

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