NOVEL SKIN FORMULATION DERIVED FROM TOBACCO WASTE

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Abstract: In Indian agriculture, tobacco has a prominent place. So it is but natural that tobacco waste or dust is generated at various stages of post-harvest processing of tobacco and also while manufacturing various products, while the chemistry of tobacco is unique with the presence of a wide spectrum of chemical compounds of which nicotine and cellulose were identified as potential chemicals. Nicotine was extracted by solvent extraction method from tobacco waste. The waste obtained after nicotine extraction was utilized for cellulose extraction. The extracted nicotine & cellulose was converted into value-added products such as nicotine pirate & cellulose acetate. Prepared nicotine picrate and cellulose acetate is characterized by Fourier transform infrared spectroscopy (FTIR). Nicotine picrate and cellulose acetate were used to prepare skin gel by Ointment slab method.

Keywords: Nicotine, Cellulose, Nicotine Picrate, Cellulose Acetate, Extraction, FTIR.

I. INTRODUCTION

Tobacco is an important crop cultivated in India and tobacco plays a vital role in the economy. In the present scenario of worldwide decline in the conventional uses of tobacco. Exploitation of the crop for extraction of phytochemicals is a viable alternative. The presence of substantial amounts of useful phytochemicals likes proteins, nicotine, solanesol, Cellulose and organic acids have enhanced the scope for alternative uses of tobacco [1], [2].

Nicotine is the source for the botanical pesticide, such as nicotine sulfate. Nicotine could be the starting material for synthesis of various nicotine derivatives as active material such as nicotinic acid, nicotine amide, & many more used in the pharmaceutical industry. Approximately 0.6 percentages (%) to 8.0 percentage (%) of nicotine are present in dry tobacco. So an integrated approach for the isolation of nicotine from tobacco waste has been proposed [3].

As rational production and processing of tobacco plant must include the entire biomass, both the main product leaves as well as stalks that remain after harvest. Residues (stalks and small leaves) and significant amounts of leaf scrap and waste generated during processing of tobacco, can serve as a very important secondary raw material from which, by final processing, a great number of products could be obtained in industry considering that these stalks contain a certain amount of nicotine [4].

On the other hand, stalk is an important secondary raw material due to its high cellulose content Thus; stalks contain 35 % to 36 % of cellulose, while the midrib has 10 % to 15 % of cellulose [5].

In older leaves, cellulose is present in a crystalline form, while in younger leaves an amorphous form of cellulose prevails. Leaves contain on average 10 % to 12 % of cellulose [6, 7]. Cellulose derivatives are widely used in bio adhesives. In various types of these formulations such as buccal, nasal, oral, vaginal, transdermal formulation alone or with combination of other polymer [8], [9], [10].

The practice of compounding requires not only the drug(s) (active pharmaceutical ingredient), but also, the excipients (pharmacological inert component) in order to obtain the final medicine. The excipients are chosen according to the characteristics of the required dosage form [11].

Each excipient exerts specific functions in the formulation, as, for instance, a diluent for hard capsules or powders, a coating agent for solid oral dosage forms, a suspending, thickening or stabilizing agent for oral liquids, ointment etc. The excipient function depends on the concentration in a particular pharmaceutical formulation [12], [13].

Ointments are semisolid systems which usually behave as viscoelastic materials when shear stress is applied. They generally contain medicaments and are intended to be applied externally to the body or to the mucous membrane. Many medicaments meant for topical application to intact or broken skin or to mucous membranes, have been presented in the form of semisolid consistency variously designated as ointments, creams, salves, pastes etc. used mainly as protective or emollient for the skin. The first step towards this goal is the screening of plants used in popular medicine. Along with other dosage forms, herbal drugs are also formulated in the form of ointment [14]

Ointments can be prepared either by mechanical incorporation or by fusion methods. Irrespective of the method employed in preparing, ointments should be smooth and free from granular or gritty particles. In compounding of ointments, the following general aspects should be considered.

If insoluble substances are to be incorporated in the ointment base, then they should be in impalpable powder form. For efficient incorporation of insoluble substances they should first be levigated with a little quantity of base to form a smooth cream and then incorporated into the remainder of the base. Water-soluble salts are best incorporated by dissolving them in a small quantity of water and then incorporating the base. Drugs soluble in ointment bases may also be incorporated by fusion (melting the highest melting point ingredient of the base and mixing the medicament into it). The remaining ingredients are then added and mixed by stirring [15]

On the other hand nicotine picrate acts as active pharmaceutical ingredient for curing skin disease [16]. Cellulose d1erivatives are employed as excipients in pharmaceutical, industrial products. This cellulose derivative has partially or completely acetylated ($COCH_3$) hydroxyl groups. Cellulose acetate is available in a wide range of acetyl levels (29-44.8 %) and chain lengths, with molecular weights ranging from 30 000 to 60 000. Cellulose acetate is used as diluent, filler and as a taste-masking agent in compounded medicines [17].

Based on these considerations, the present work investigates the extraction of cellulose and nicotine from agriculture wastes and extracted cellulose and nicotine are chemically modified to their derivative known as cellulose acetate and nicotine picrate. Prepared derivatives of nicotine and cellulose was characterized by Fourier transform infrared spectroscopy (FTIR). The ointment formulation was prepared by using nicotine picrate as active pharmaceutical ingredient and cellulose acetate as drug binder.

II. MATERIAL AND METHOD

Tobacco was obtained from Mahi tobacco, Anand. Sodium hydroxide and solvent use of laboratory grade alcohol were purchased from Atul chemical, Anand.

Percentage of nicotine

Weight out finely grounded tobacco powder in a known quantity. Add it into 250 milliliter (ml) iodine flask along with 5 percentages (%) acetic acid solution. Swirl the content until the tobacco waste is wetted out. Add 1:3 mixer of benzene: chloroform and 36 % Sodium hydroxide solution to iodine flask shake the flask thoroughly for 20 minutes (min). Take 25 ml aliquots of filtrate into each of 250 ml flask. Add two drops crystal violet in a flask and titrate with 0.025 Normality (N) Perchloric acid to the green end point.

% Nicotine = (X x N x 32.4) / sample weight

X = Burette Reading (18.2 ml)

N = Normality of Perchloric acid (0.025 N)

Extraction of nicotine by chloroform

Accurately weigh 20 grams (g) of sample in thimble & put in a sohxlet assembly on a round bottom flask, Add 150 ml of chloroform as solvent. Now put the assembly in heating mental and carried out extraction for refluxing temperature for 6 hours (h). After completion of an extraction mixture of nicotine and chloroform is separate using simple distillation.

Preparation of nicotine picrate

The above extracted nicotine was further used for making nicotine salt of picrate known as nicotine picrate by reacting the extracted nicotine with picric acid. 2 moles of picric acid are dissolved in ethanol to this solution 1 mole of nicotine was added immediately exothermic reaction took place. On cooling for 2 h in ice bath crystallization began. After 5 h the needle-like crystal were filtered to get the Nicotine picrate.

Extraction of cellulose

Tobacco waste after extraction of nicotine was used as a source of cellulose. Weigh 35 g sample of the tobacco waste (after extraction of nicotine) was stirred with 700 ml nitric acid 1.0 molars (M) at room temperature for 24h, filter the raw material and wash residue. The wet material was subsequently dried in an oven at 100 degree Celsius (°C) for 24 h to purify extracted cellulose from silica and ligline it was extracted with 1.0 M Sodium hydroxide for 24h at room temperatures. It was then filtered using suction filtration. The solid was washed several times using distilled water. The solid was treated with an alkali solution of sodium hydroxide (6.0 M) for 6 h. The solid was then filtered to be used for cellulose extraction. The filtrate was neutralized with acid at a room temperature using sulfuric acid (5.0 M) under continuous stirring until the constant potential of hydrogen (pH) in the range of 5–6 was reached. The resulting suspension hydrolyzed material was then separated by vacuum filtration and washed roughly with distilled water to get cellulose.

Preparation of cellulose acetate

10.0 g of cellulose was added to a solution of 0.5 g of sulfuric acid in 50 ml glacial acetic acid.Uniform wetting of the cellulose is ensured by stirring with a glass rod, the closed bottle is then allowed to stand for 1 h at room temperature. After this pre-treatment, a mixture of 50 ml 95 % acetic anhydride and 20 ml glacial acetic acid is added and the bottle is closed and placed in a water bath at 50 °C. The cellulose dissolves after 15 min, the reaction being completed after another 15 min this is called “primary solution”.

In primary solution 50 ml 80 % acetic acid at 60 °C are carefully stirred into one half of the primary solution in order to destroy the excess acetic anhydride. The solution is held at 60 °C for another 2 h, and then poured into beaker; 50 ml of water is carefully stirred. After the addition of 200 ml water, cellulose acetate precipitates as a white, crumbly powder.

Determination acetyl contains and degree substitution via titration

Shake 5 g of the sample, in a 250 ml Erlenmeyer flask with 150 ml of water. Stopper the flask and allow it to stand for 3 h filter off the cellulose acetate and wash it with water. Titrate the combined filtrate and washings with 0.01 N sodium hydroxide solutions, using phenolphthalein indicator solution. Run a blank determination on the water, using the same volume as was used in extracting the sample.

Calculate the percentage of acidity as free acetic acid as follows:

$$\% \text{ Acetic acid } = \frac{(A - B)x\ N\ x\ 0.06\ x\ 100}{W}$$

Where,

A = Sodium hydroxide solution used to titrate the sample, ml

B = Sodium hydroxide solution used to titrate the blank, ml

N = Normality of the sodium hydroxide solution,

W = Sample used (g)

Degree of substitution calculates on the basis of % acetic acid contain according on below equation.

$$\% \text{ Degree of substitution } = \frac{3.86\ x\ \% \text{ Acetic acid}}{102.4\ x\ \% \text{ Acetic acid}}.$$

Preparation of ointments

Ointment was prepared by the mixing process. First binder mixed with plasticizer to avoid formation of lumps of after proper mixing of binder and plasticizer add API (active pharmaceutical ingredient). After that mixed with the base generally use as petroleum jelly.

Table 1: composition of ointment

Name of the substance	Weight (g)
Nicotine picrate (API)	0.63 g
Cellulose acetate (binder)	1.26 g
Glycerine (plasticizer)	1.00 g
Petroleum jelly (base)	18.11 g
Total	21.00 g

Fig. 1: Nicotine picrate (API)

Fig. 2: Cellulose acetate (binder)

Fig. 3: Ointment formation

FTIR Spectroscopy

Fourier transform infrared spectroscopy (FTIR) is a technique which is used to obtain an infrared spectrum of absorption, emission, photoconductivity or Raman scattering of a solid, liquid or gas. An FTIR spectrometer simultaneously collects high

spectral resolution data over a wide spectral range. This confers a significant advantage over a dispersive spectrometer, which measures intensity over a narrow range of wavelengths at a time. Infrared spectroscopy, IR radiation is passed through a sample. Some of the infrared radiation is absorbed by the sample and some of it is passed through (transmitted). The resulting spectrum represents the molecular absorption and transmission, creating a molecular fingerprint of the sample. Like a fingerprint, no two unique molecular structures produce the same infrared spectrum. This makes infrared spectroscopy useful over several types of analysis. The resulting products were characterized by FTIR spectroscopy using Perkin Elmer spectrum GX instrument, by the KBr pallet method.

III. RESULT & DISCUSSION

Percentage of nicotine

Table 2: Percentage of nicotine

No.	Tobacco waste sample	Percentage of nicotine
1	Sample 1	6.02 %
2	Sample 2	5.90 %
3	Sample 3	6.02 %

Percentage of nicotine in the sample tobacco was found 6.02% was obtained by performing titration with Perchloric acid against the sample tobacco treated with various reagents.

Extraction of nicotine

The extraction of nicotine from tobacco waste was carried out successfully by solvent extraction method by using sohxlet assembly; the extracted nicotine was evaluated by its physical properties such as color, boiling point and solubility. The nicotine obtain was yellow-brown/oily liquid that is readily soluble in alcohol, it was miscible in water and the boiling point obtain was 240^0C, which conform that extracted martial was nicotine.

Optimization of nicotine extraction was carried by varying amount of solvent (chloroform), temperature and time of reaction which is shown in below mention tables respectively.

Table 3: Effect of chloroform

No.	Chloroform (ml)	Temperature (^{0}C)	Time (h)	Result (nicotine in g)
1	50	60	6	0.85
2	100	60	6	1.00
3	150	60	6	1.20
4	175	60	6	1.20

In the above table 3, amount of solvent (chloroform) is varied from 50 ml to 175 ml by keeping time and temperature constant at 6 h and 60 ^{0}C, respectively. So from the above table, we can conclude that the optimum amount of solvent required for extraction of nicotine was 150 ml. The volume of solvent has a significant effect on extraction efficiency from the above table; we can observe that as the volume of solvent increases the amount of extracting nicotine increases. The possible reason for the increase efficiency with the increasing amount of the solvent might be, due to the increase in swelling of tobacco waste material by solvent, which increase the contact surface area between the tobacco waste and solvent. So the extraction of nicotine compound from the tobacco waste material is directly related to the amount of solvent.

Table 4: Effect of temperature

No.	Chloroform (ml)	Temperature (^{0}C)	Time (h)	Result (nicotine in g)
1	150	70	6	0.92
2	150	65	6	1.09
3	150	60	6	1.2
4	150	55	6	0.45

In the above table 4, temperature was varied by keeping the amount of solvent and reaction time constant. The temperature was varied from 55 ^{0}C to 70 ^{0}C at an interval of 5 ^{0}C but the best result was obtained at 60 ^{0}C. The extraction temperature was another important influencing the extraction of nicotine, the above table indicates that a significant increase in extraction of nicotine to increase in temperature. This is due to increase solubility and diffusion coefficients of nicotine; decreased solvent viscosity; as well as enhanced mass transfer and penetration of solvent in to the tobacco waste, thus accelerating the whole extraction on other hand heating might soften the tobacco waste tissue, so nicotine might be easily extracted, so the moderate temperature of extraction is 60 ^{0}C but at higher temperature 70 ^{0}C the yield was lower because solvent might be started vaporized which effect directly the loss of solvent to solid ratio.

Table 5: Effect of time

No.	Chloroform (ml)	Temperature (^{0}C)	Time(h)	Result (nicotine in g)
1	150	60	2	0.79
2	150	60	4	0.92
3	150	60	6	1.20
4	150	60	8	0.95

In above table 5, show that reaction time was varied by keeping the amount of solvent (chloroform) and temperature constant. Reaction time varies from 2 h to 8 h it was varied at intervals of 2 h the optimum reaction time was 6 h. The selection of an appropriate extraction time was the final step in a series of single factor experiments. The above table shows that nicotine extracted increased gradually with increase in time, these phenomena could be explained by the fick's second law of diffusion, predicting that a final equilibrium between the solute concentration in the solid matrix and in the solvent might be reacting after a certain time, the leading deceleration in the extraction yield. More over prolong the extraction time, increase the chance of decomposition of the desired compound. So the moderate time was 6h

So it can be concluded that optimum temperature was 60 ^{0}C with 6 h of extraction time by using 150 ml of chloroform as extracting solvent for the fruitful extraction of nicotine from tobacco waste.

Nicotine picrate

Extracted nicotine from tobacco waste was converted in salt of nicotine as the nicotine picrate by using picric acid as reagent.

Table 6 Effect of concentration of picric acid

No.	Concentration of picric acid (M)	Result (nicotine picrate in g)
1	0.5	0.52
2	1.5	0.85
3	2	1.15
4	2.5	0.90

In above table 6 concentrations of nitric acid were changed from 0.5M to 2.5M, best result was obtained at 2M while increasing the concentrations yield started to decrease the reason behind this might be Synthesis of nicotine picrate is exothermic reactions; increasing the temperature decreases the solubility of the solute. This is because heat energy is released when the solute dissolves in solution. Increasing temperature introduces more heat into the system. So, according to Le Chatelier's Principle, the system will adjust to this excess in heat energy by inhibiting the dissolution reaction

Extraction of cellulose

Tobacco waste after extraction of nicotine was used as a source of cellulose, which was extracted by solvent extraction method by using varied reagents such as nitric acid, sodium hydroxide and many more. The extracted cellulose evaluated by its physical properties such as appearance, melting point and density. The extracted martial was white powder with melting point 265 ^{0}C and insoluble in water with a density of 1.43 g/cm^3 which conform that extracted martial was cellulose.

Table 7: Effect of concentration of nitric acid

No	Concentration of nitric acid (M)	Time (h)	Result (Cellulose obtains in g)
1	0.5	24	1.25
2	1.0	24	3.87
3	1.5	24	2.15
4	2.0	24	1.85

In above table 7, concentration of nitric acid varied from range 0.5 M to 2.0 M by keeping time as constant the maximum yield was obtained when the concentration of nitric acid was 1.0 M. Because the chemical treatment of cellulose using a nitric acid solution to remove most of lignin and solubilized hemicellulose, while acid hydrolysis breaks the amorphous cellulose. The effect of varying nitric acid concentration on tobacco waste will result in increasing the cellulose content from tobacco waste, but the further increasing in nitric acid concentration result in lowering the cellulose content as reflected in above table, however this method is based on the insolubility of cellulose in water and it's resistance to action of diluted acid, the sample was stated to degrade at higher concentration. In fact, when the solvent is saturated on the desired compound, the cellular phenomenon of diffusion stop and there has stabilization rate of extracting compound or decreased.

Table 8: Effect of time

No	Concentration of nitric acid (M)	Time (h)	Result (Cellulose obtain in g)

1	1.0	12	1.65
2	1.0	24	2.35
3	1.0	36	3.87
4	1.0	48	3.87

In the above table 8, experimental result showed that the extraction time (12,24,36,48 hour) did not uniformly influence the recovery of cellulose above table reflect that 36 h is the optimum reaction time because as the time increases contact between solute and solvent increase which lead to accelerate the extraction yield. On the other hand, increased extraction time is uneconomical as it does not any chance in extraction yield.

So it can be said the optimum extraction of cellulose was carried out at 36 h by using 1.0 M solution of nitric acid as extraction agent.

Cellulose acetate

Cellulose acetate was synthesized from extracted cellulose by reacting with various reagents, and there optimization of cellulose acetate was carried out as mention below. The cellulose acetate obtain was off white solids that is readily soluble in alcohol, it was miscible in water and the boiling point obtain was 240^{0}C, which conform that extracted martial was nicotine.

Table 9 Effect of acetic acid

No	Acetic acid (ml)	Time (h)	Temperature (^{0}C)	Degree of Substitution
1	30	2	60	0.62
2	40	2	60	0.79
3	50	2	60	0.87
4	60	2	60	0.88

Synthesis of cellulose acetate was carried out at variable amount of acetic acid from 30-60 ml as shown in table 9. But the degree of substitution (DS) increased as a result of increasing the amount of acetic acid up to 50 ml. There was no more change was observed degree of substitution when acetic acid was used in the amounts of 50 ml and 60 ml. So we found 50 ml acetic acid is the best proportion. Increase in amount of acetic acid leads to the alkali degradation of cellulose. The lower amount of acetic acid leads to a lower number of free hydroxyl group deprotonated to form alkoxide which was resulted in the lower value of degree of substitution.

Table 10 Effect of time

No	**Acetic acid (ml)**	**Time (h)**	**Temperature (^{0}C)**	**Degree of Substitution**
1	**50**	**0.30**	**60**	**0.59**
2	**50**	**1**	**60**	**0.65**
3	**50**	**2**	**60**	**0.87**
4	**50**	**3**	**60**	**0.87**

In above table 10 optimization of cellulose acetate was carried out by varying times from 0.30 h to 3 h duration, by keeping other limits constant. It can be settled from the table that degree of substitution, improved to increase in time from 0.30 h to 3 h. But the degree of substitution was almost same at the end of 2 h and 3 h. So we selected 2 h is the best reaction time. Besides, carrying out the reaction for 3 h (i.e. One hour more) was likely to increase the production cost.

Table 11 Effect of temperature

No	**Acetic acid (ml)**	**Time (h)**	**Temperature (^{0}C)**	**Degree of Substitution**
1	**50**	**2**	**40**	**0.52**
2	**50**	**2**	**50**	**0.75**
3	**50**	**2**	**60**	**0.87**
4	**50**	**2**	**70**	**0.86**

In above table 11 synthesis of cellulose acetate was carried out by changing temperature in the range of 40-70 ^{0}C, keeping other limits constant. It can be perceived from the above table that degree of substitution, improved to increase in temperature from 40 to 70 ^{0}C. But the degree of substitution obtained at 60 ^{0}C was almost same as obtained at 70 ^{0}C. Beside maintaining temperature higher than 60 ^{0}C was likely to increase the production cost. So we selected 60 ^{0}C as the best reaction temperature.

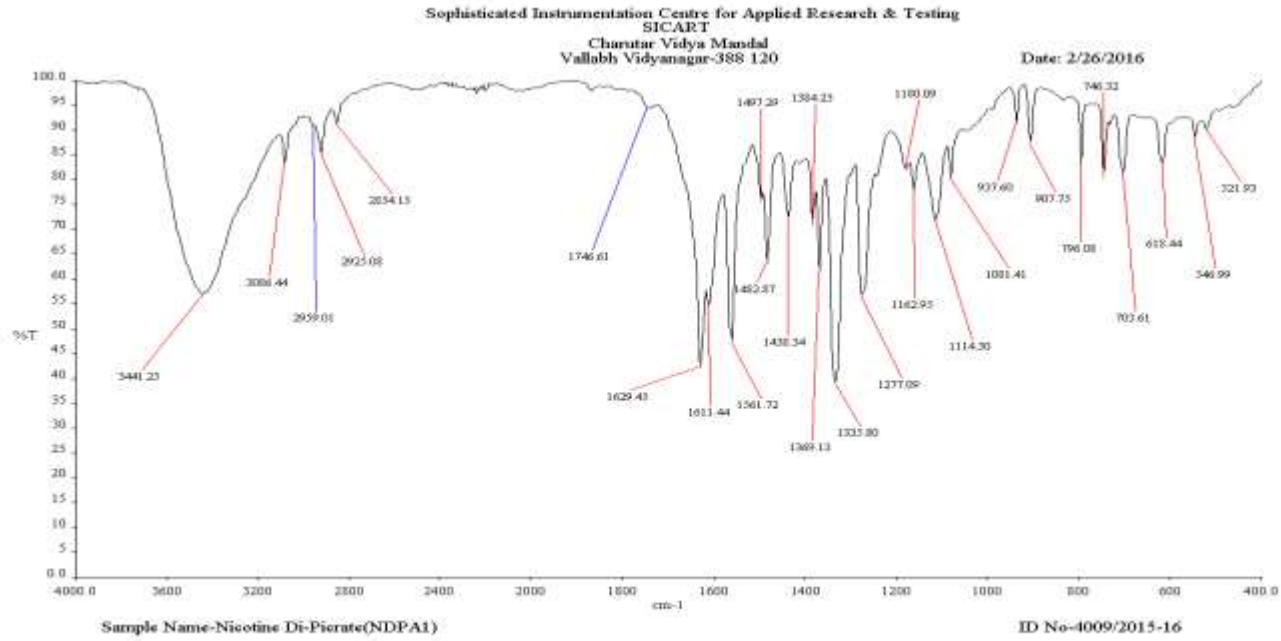

Fig.4: IR spectrum of nicotine Di- Picrate

The IR spectrum of picric acid was shown in Figure 4. 4.907 cm^{-1} and 703 cm^{-1} is mono substituted pyridine cycle, 1629 cm^{-1} is aromatic C=N, 1300 TO 1400 cm^{-1} Nitro group, and 3441 cm^{-1} is phenol group. Which indicate the nicotine picrate is successfully preparing and conform.

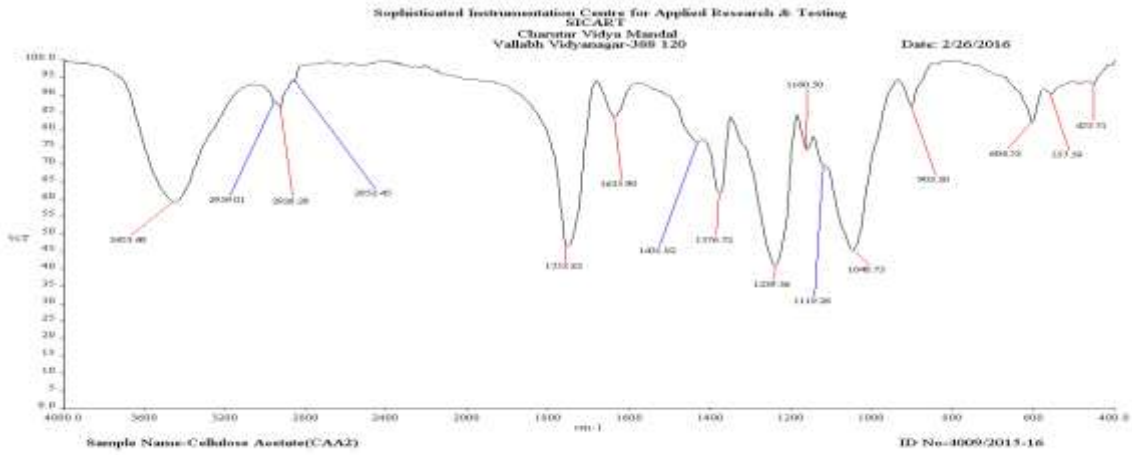

Fig. 5: IR spectrum of Cellulose Acetate

The IR spectrum of cellulose acetate was shown in Figure 5. 1753 cm^{-1} is starching of carbonyl group C=O of the acetyl group (-$COCH_3$) in cellulose acetate which also conform that cellulose acetate is successfully prepared.

Physical properties of Ointments

In the formation of semi-solid dosage forms mixing is the key process to avoid problems like formation of lumps. Prepared ointments were evaluated form, appearance, solubility. An appearance was yellow gel like material (no formation of small solid particle.). Ointment formed was partially soluble in methanol, water and insoluble in acetone, Carbon tetra chloride.

IV. CONCLUSION

The extraction of nicotine and cellulose from tobacco was carried out successfully. Both extracted nicotine and cellulose was used to prepare their value-added derivative (nicotine picrate and cellulose acetate) successfully prepared and it is confirmed by FTIR. Nicotine picrate can be used as an active ingredient for curing various skin diseases. The best result for the degree of substitution 0.87 obtained by carrying reaction at room temperature for 3 hours, by titrated with sodium hydroxide. This cellulose acetate was widely used in pharmaceutical formulation of ointments. Ointments prepared by the ointment slab method. Prepared ointments were yellow in appearance, partially soluble in methanol, water and insoluble in acetone and carbon tetra chloride.

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