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A MINI REVIEW ON SOLANESOL: A POTENTIAL PHYTOCHEMICAL FROM TOBACCO SCRAP & A NEW METHOD FOR THE EXTRACTION OF SOLANESOL

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ABSTRACT

Solanesol is the starting material for many biochemicals, including Co-enzyme Q10 and vitamin-K analogues. Solanesol a naturally occurring trisesquiterpenoid (C45) alcohol, all transnonaprenol, of tobacco is one of the important precursor of the tumorigenic polynuclear aromatic hydrocarbons (PAHs) of tobacco smoke. The present paper gives an account of updated information on its phytochemical, analytical. The review reveals that solanesol has been isolated and quantified by large number of analytical methods and with solanesol as its primary material. These reports are very encouraging and indicate that solanesol should be studied more extensively for its therapeutic benefits.In the present research study, an important method has been introduced for the extraction of solanesol from the Flue-cured tobacco leaves.

Key Words: Solanesol, *Nicotiana tabacum,* Phytochemical, Thin Layer Chromatography.

INTRODUCTION

Solanesol is commonly found in plant leaves and is one of the ingredients present in tobacco, potato leaf and mulberry leaves. Tobacco especially has up to 0.85-3.75% of Solanesol. It is also found widely distributed in higher plants of Solanaceae family like *Solatium melongena, Solatium lycopersicum, and Capsicum annum.* These contain Solanesol to an extent of 0.30 to 0.40%, while *Datura stramonium, Solanum nigrum, Nicandra physaloides, Cestrum nocturnum and Solanum xantho carpum* contain Solanesol to an extent of 0.05 to 0.25%. Solanesol (C45H74O) is a trisesquiterpenoid alcohol which was first isolated from tobacco. Solanesol is widely distributed in plants of Solanaceae family. Nicotiana genus (tabacum) is the richest source of solanesol, other members of the family containing solanesol include pepper plants, potato plants, tomato plants and egg plants. Some of the chemical compounds related to solanesol are Solanesyl acetone, Solanesyl bromide, Phytol, Solanofuran, Solanesol Acetate, Solanesol 3, 5-Dinitrobenzoate, Solanesol 3-Nitrophthalate, Solanesol p-Phenylbenzoate1, 4etc. Solanesol is considered to be a good source of a large number of bioactive substances and is the starting material for many high value biochemicals, including Co-enzyme Q10 and vitamin-K analogues. Solanesol is also a potentiating agent in many medicines [1, 2].

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Analysis of solanesol

Absence of selective UV absorption precludes UV spectrophotometry. TLC densitometry offers a most convenient and rapid method for solanesol determination. TLC densitometry can best give semi-quantitative estimates because of the above reasons and also due to the decomposition of solanesol on TLC plates, making GLC or HPLC techniques imperative for accurate and reliable analysis of solanesol. Low volatility, poor Flame Ionization Detector (FID) response and formation of solanescenes by the thermal dehydration of solanesol under the operating conditions of GLC, the compound requires derivitization either as corresponding saturated alcohol by dehydrogenation. However, HPLC appears to be a preferred technique because of the ease of analysis, particularly the avoidance of derivitization. Different

HPLC conditions are reported in the literature for analysis of the compound: Zorbax-Sil column, hexane: isopropyl ether (70:30) as eluent; Resolve C18 column, gradient elution with methanol: acetonitrile; Partisil 5 column, hexane; diethyl ether (93:7) as mobile phase; C_{18} column, methanol as mobile phase

Biological importance

Solanesol is a terpene compound and an important intermediate of nutrients such as vitamin K_2 and coenzyme Q_{10}.

It is the starting material for many high-value bio-chemicals as vitamin-k analogues and coenzyme Q_{10}, which is virtually present in every cell in the human body and is known as the "miracle nutrient" as it can be also used as anti-aging agent. It is also a potentiating agent in these medicines. After introducing "solanesol" radical into the structure of some medicines, the effect are increased distinctly [3-8].

Solanesol can counteract the bacteria, diminish inflammation and hemostasis. It also has strong activity of counteracting the cancer.The anti-cancer drug N-solanesyl-N, N-bis (3, 4-dimethoxybenzyl) ethylenediamine (SDB-ethylenediamine), synthesized by incorporating Solanesol materials, was 5 times more effective than its parent compound.

Highly purified Solanesol is a major intermediate to synthesize CoQ_{10}, vitamin K_2 and raw material medicine. Western medical researchers found that highly purified Solanesol itself can be directly used as a clinical drug, main clinical uses are as follows: anti-heart failure, treatment of liver injury, as well as adjuvant therapy for cancer.

"India Journal of Medicine" reported that many hospitals in India have conducted clinical contrast tests of "Highly purified Solanesol preparation as therapeutic agents and anti-cancer drugs".

In addition, $CoQ_{10,}$ which is synthesized by use of Solanesol, has also been highly concerned in European and American medical circles, and the findings have constantly been covered by the press: It can promote the reaction of Oxidative phosphorylation and synthesis of Adenosine Triphosphate (ATP), it can be used as cell activator of metabolism and respiration, and helps to strengthen human body's immune system.

N-solanesyl-N,N-bis (3,4- dimethoxy benzyl) ethylene diamine (SDB-ethylene diamine) inhibits the colony formation of multidrug resistant mutant cell lines derived from Chinese hamster V79 (V79/ADM) and human hepatoma PLC/PRF/5 (PLC/COL) cells to a greater extent than that of the parental cells when combined with other derivatives useful as antitumor agents. It potentiated the cytotoxic activity of almost all kinds of drugs tested including adriamycin (ADM), actinomycin D, Vincristrine, Cytoxinearabinoside and 5-fluorocil urea (5-FU). Isomeric solanesol (2-Z) prepared from solanesol was reported as antihypertensive, antihyperlepidemic and antitumor-agents.

PHYTOCHEMICAL AND ANALYTICAL REVIEW

Rowland *et al*. (1956) first reported the presence of solanesol in tobacco. They reported that solanesol levels of green (freshly harvested) tobacco leaf were 0.3% of the total leaf dry weight, and that solanesol levels of both unaged, flue-cured tobacco leaf and aged, flue-cured tobacco leaf appeared to increase slightly to about 0.4% of the total dry [9].

Severson *et al.* (1977) reported solanesol concentrations in Maryland tobacco of slightly over 2% of total leaf dry matter. An Eastern Carolina flue-cured variety showed concentrations of approximately 3% of dry matter, while two burley varieties had approximately 1% and 2% solanesol, respectively [10].

Chamberlain *et al*. (1990) reported total solanesol concentrations in six flue-cured tobacco varieties ranging from 1.9% to 2.8% (dry basis). Free solanesol in these six varieties ranged from1.3% to 2.5% of total leaf dry weight [11].

Later research determined that the apparent increase in solanesol in cured leaves observed by early researchers was primarily due to the release of bound solanesol, in the form of esters, through the curing process. Addition of low concentrations of sodium hydroxide to the extraction solution has produced a 15-20% increase in solanesol recovery. Both free and bound forms of solanesol are found primarily in the chloroplasts of tobacco leaves.

Zhao *et al*. (2007) used high performance liquid chromatography (HPLC) to measure solanesol concentrations in various parts of the tobacco plant. They found that leaf solanesol concentrations were 6.8 times greater than in the stalks. The ratio between leaf concentrations and concentrations in other plant parts (i.e., flowers, seeds, fruits, and roots) was even greater [12].

Shefali Srivastava et.alsynthesiszed several natural products like3-(2-Methoxy –phenyl)-acrylic acid 3,7,11,15,19,23,27,nonamethyl-hexatriaconta-2,6,10,14,2,-nonaen-1-yl ester and other ester derivatives derived from solanesol as wound healing agents[13].

Masako Asahina *et al* invented a process for the manufacture of Solanesol which is an all trans type isoprenyl alcohol [14].

Toyoda *et al* (1969) isolated solanesol from acetone extract of dried silkworm faeces. An acetone extract was saponified with methanolic potassium hydroxide and unsaponified matter was treated for isolation of solanesol [15].

Okamato Y *et al* (1994) published the work for the synthesis of solanesol. They used geranyl acetone as starting material followed by sequence of reactions for the synthesis [16].R. Ruegg et al (1960) used farnesylgeranyl linalool and phosphorus tribromide followed by number of stages to synthesize Solanesol [18].

MATERIALS AND METHODS

EXPERIMENTAL

Meltingpoint were recorded on an electrically heated melting point apparatus and are uncorrected. The $\lambda_{max}$of the compounds was measured by UV-VIS spectrophotometer (UV –Pharma Spec 1700 Shimadzu).The IR Spectra were recorded on Perkin-Elmer IR Spectrometer 8400S using KBR disc. The 1HNMR Spectra were obtained on a Bruker DRX-400MH_Z Spectrometer in $CDCl_3$ using TMS as internal standard and chemical shifts are expressed in δ scale.FAB mass spectra were recorded on a JEOL SX 102/DA 6000 mass spectrometer using Argon/Xenon (6KV, 10Ma) as the FAB gas.EI mass spectra were recorded on JEOL JMS-D-300 spectrometer with the ionization potential of 70 e V and ES mass on Quantro –II, micromass instrument. Silica gel (60-120 mesh) for column chromatography was used. Room temperature mentioned are in the range between 20-40^{0}C unless stated otherwise.

Chemicals and materials

Analytical standards from Sigma Aldrich (>90%) are considered for solanesol standard and solvents such as Hexane, Ethyl acetate, Ethyl alcohol, Isopropanol of HPLC grade chemicals like Potassium Hydroxide , Silica gel and Acetonitrile have been employed for extraction (by chromatography), identification (by TLC) .

Plant Materials

The dried leaves of *Nicotiana tobaccum* collected from centre for tobacco research, Rajmundry, Andhra Pradesh and were authenticated by a botanist, Professor, Dr.CH. Manohara chary, Department of Botany, Osmania University, Hyderabad.

Extraction of solanesol

In the present research study, an important method has been introduced for the extraction of solanesol from the Flue-cured tobacco leaves. In this method the tobacco leaves were dried at 70°C for 3 hrs, grounded and passed through a 40-mesh sieve the grounded leaf powder (1000 g) were extracted by employing n-hexane (5 liters) on a water bath at 50°C, refluxed for 3 hrs and filtered. The residue was re-extracted successively with n-hexane. The hexane extracts were mixed and concentrated by rotary vacuum evaporator at 40°C. The pasty residue was saponified with 10% methanolic potassium hydroxide (50 ml) and then extracted with hexane, washed free of alkali, concentrated and again dried by rotary evaporation and it was eluted with 9:1 hexane: Ethylacetate by column chromatography to get pure solanesol.

Schematic representation

Powdered tobacco leaves+Hexane
↓
Saturated residue+4 times volume of Methanolic KOH
(heated on a water bath between 50- 60^{0}C)
↓
Clear metanol layer was separated and cooled
↓
Solanesolis solidified (Elutedwith 9:1 hexane: Ethylacetate by column chromatography)
↓
90% pure Solanesol

Silica gel low-pressure column chromatography

Silica gel low-pressure column chromatography technique has been developed for the purification of the solanesol. In the Present method, the crude solanesol dissolved in hexane at a ratio of 10:1 (v/w) of hexane-to-crude solanesol. It has been run on a silica gel column (30 cm×2.0 cm i.d.), which was preconditioned with n-hexane. The column was eluted with n-hexane : ethyl acetate (9:1, v/v). The eluent was collected in fraction of 5ml and tentative identification has been carried out using TLC. The fractions containing solanesol was dried by rotary evaporation.

TLC detection

Silica gel plates were activated at 120°C for 1h before used. 10µl of each fraction collected from column chromatography along with solanesol standard solution was loaded to the marked points about 10mm from the bottom of silica plate. The plates were developed in hexane: ethyl acetate (9:1v/v) at room temperature and the separated spots were visualized by iodine fume. Ingredients of each fraction were compared with standard for identification. The solanesol has been identified by TLC which is presented in the figure 5.

RESULTS

Table 1. Physical and chemical properties related to solanesol

Synonyms	Nonaisoprenol, betulaprenol9, betulanonaprenol
Chemical family	Unsaturated polyisoprenoid
Chemical name	(2E,6E,10E,14E,18E,22E,26E,30E)-3,7,11,15,19,23,27,-31,35-Nonamethyl-2,6,10,14,18,22,26,30,34-Hexatriacontanonaen-1-ol
Molecular Formula	$C_{45}H_{74}O$
Percent Composition	C 85.65%, H 11.82%, O 2.54%
Molecular Weight	631.07grams

Appearance	Rough solanesol is brown and stringy paste matter. Refinement solanesol is white powder
Solubility	It is soluble in organic solvents but insoluble in water
Melting point	33^0 - 42.5^0C
Storage	The product is stable stored at 2-8 °C and in a damp proof, airtight, light resistant area for at least two years
Thin layer chromatography	Mobile phase used is n-hexane:Ethyl acetate(9: 1) R_f value is found between 0.36- 0.40

Table 2. Physical data

Molecular Formula	$C_{45}H_{74}O$
Percent Composition	C 85.65%, H 11.82%, O 2.54%
Molecular Weight	631.07grams
Appearance	Rough solanesol is brown and stringy paste matter. Refinement solanesol is white powder
Solubility	It is soluble in organic solvents but insoluble in water.
Melting point	36^0C
TLC	

Fig 1. Solanesol in tobacco

Fig 2. Structure of Solanesol

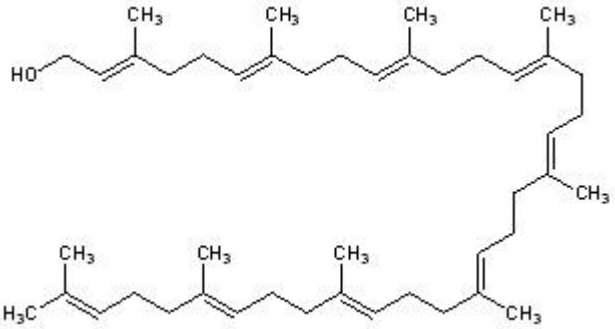


Fig 3. Structure of Co enzyme Q_{10}

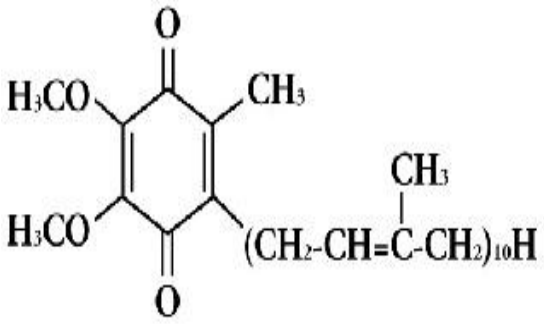


Fig 4. Silicagel column chromatography

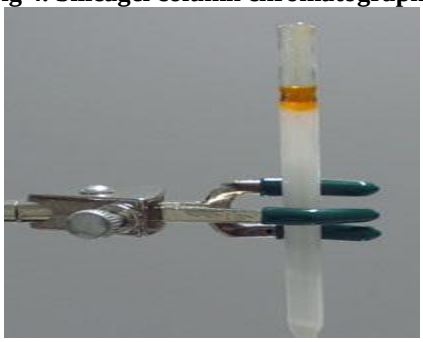


Fig 5. TLC chromatogram of Solanesol

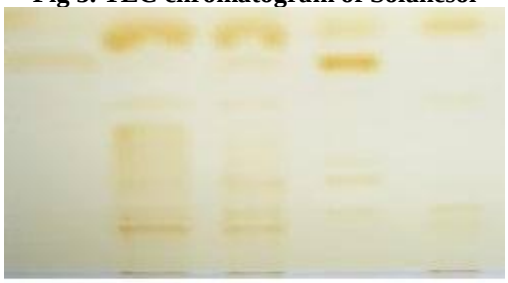
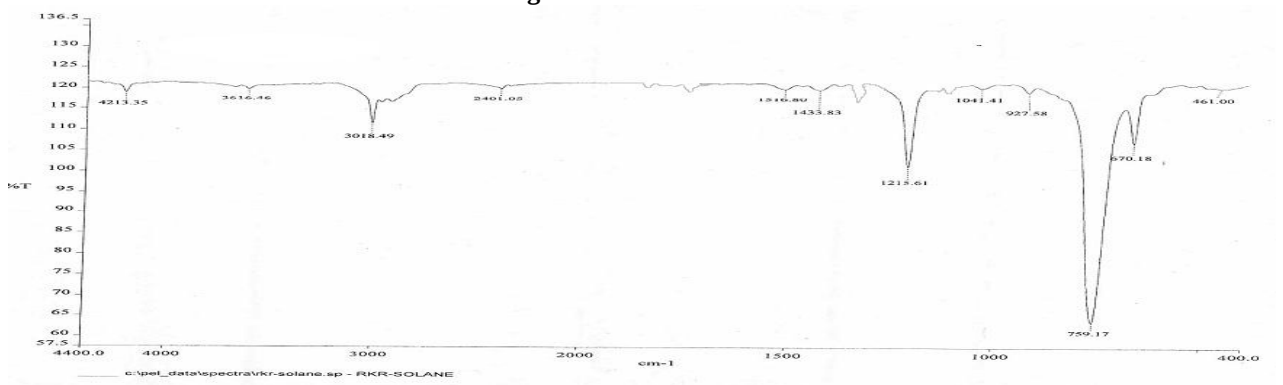


Fig 6. FTIR of Solanesol



CONCLUSION

Solanesol is the starting material for many high-value bio-chemicals as vitamin-k analogues and coenzyme $Q_{10.}$ The extraction of solanesol is done from Flue-cured tobacco leaves by selecting eco friendly and easy method by using various chemicals lead to production of more yield of solanesol compared to natural and synthetic production. Physico chemical data, FTIR data shown that the isolated compound may be solanesol. However furtherly, it can be confirmed by NMR and Mass Spectra.

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