ISOAMYL SALICYLATE: SYNTHESIS AND USE IN BEAUTY SOAP AS A FRAGRANCE

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***ABSTRACT**: Synthesis of isoamyl salicylate was subjected to done by the reaction of isoamyl alcohol with salicylic acid using different catalysts. Only the results were obtained in case when sulfurac acid was used as a catalyst. Total yield was 95%. The synthesized isoamyl salicylate was used in the preparation of beauty soap. Different tests were done for the analysis of Soap. The purity of the "isoamyl salicylate" was determined by the help of "Gas Liquid chromatography (GLC)". The purity of the prepared sample was 67.7175%.*

1. INTRODUCTION

Salicylic acid or 2-hydroxybenzoic acid, $C_6H_4(OH)CO_2H$, a colorless, crystalline organic carboxylic acid that melts at 159^{o}C is soluble in ethanol and ether but is slightly soluble in water. It is prepared commercially by heating sodium phenolate (the sodium salt of phenol) with carbon dioxide under pressure to from sodium salicylic, which is treated with sulfuric acid to liberate salicylic acid. Salicylic acid and its derivatives are toxic when consumed in large amounts. Sodium salicylate is used to a small extent as a food preservative and as an antiseptic in mouthwashes and toothpastes. The major use of salicylic acid is in the preparation of its ester derivatives; since it contains both a hydroxyl (-OH) and a carboxyl (-CO_2H) group, it can react with either an acid or an alcohol. The hydroxyl group reacts with acetic acid to from the acetate ester, acetylsalicylic acid. Several useful esters are formed by reaction of the carboxyl group with alcohol. The methyl ester, methyl salicylate (also called oil of wintergreen since it produces the fragrance of wintergreen), is formed with methanol; it is used in food flavorings and in liniments. The phenyl ester, phenyl salicylate, or salol, is formed with phenol; it is used in medicine as an antiseptic and antipyretic. This ester hydrolyzes, not in the acidic stomach, but in the alkaline intestines, releasing free salicylic acid. The menthyl ester, menthyl salicylate,which is used in suntan lotions, is formed with menthol. lsoamyl salicylate is used in perfumes and fragrances [1]. Perfume and fragrance compositions containing salicylic acid esters, of which the ester function is derived from secondary or primary branched chain, saturated aliphatic alcohols containing 6C several salicylates are being used as fragrance ingredients [3]. Most fragrance salicylates are volatile. Approximately 3000 different fragrance chemical are currently used in the perfume industry in which several are the esters of salicylic acid with alcohol, and are often combined to create characteristic scents [8]. Salicylates of salisylic acid with alcohols may have adverse effects on humans [3, 5 & 8]. Such effects may be categorized according to localisation (e.g. to the skin or respiratory organs) or pathophysiology (e.g. type of immunological response).The pathophysiology, terminology, and epidemiology of adverse reactions related to the skin are well established [3, 5]. Adverse skin reactions are predominated by contact allergy to salicylates, one of the commonest causes of contact allergy in both the general population [9, 10] and in eczema patients [11]. The adverse effects of salicylates related to the respiratory organs are not well described and the underlying pathophysiology of the symptoms is unclear. In a single case, anaphylaxis has been reported after spraying perfume in the eyes [13]. salicylates may also cause occupational asthma [6,12] and elicit symptoms in individuals with asthma and rhinitis [10,12]. However, lower respiratory symptoms associated with perfume and other fragrance products are also frequent among non-asthmatic andnon-allergic individuals [13, 14].

Numerous plants produce isoamyl salicylate in very small amounts [15]. It is a toxic compound. Aside from its toxicity, isoamyl salicylate may also be used by plants as a pheromone to warn other plants of pathogens such as tobacco mosaic virus [16]. It is manufactured on a small scale for use in perfumes and as a food flavouring, as well as being a component of biodiesel. It has a scent similar to pineapple [17] which is not detectable by all people.

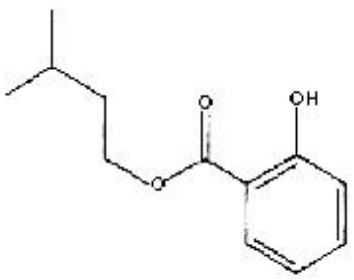

Fig 1 Structure of Isoamyl Salicylate

It is used in small amounts as a flavoring agent. It is also used to provide fragrance to various products. If applied in too high quantity it can cause stomach and kidney problems. It is commonly used as bait to attract and collect the bees for study [18]. Isoamyl salicylate also has the ability to clear plant or animal tissue samples of color, and as such is useful for microscopy and ammunohistochemistry when excess pigments obscure structures or block light in the tissue being examined. Isoamyl salicylate is also used in some kinds of chewing gum and candy, as an alternative to

the more common peppermint and spearmint oils [19]. Isoamyl salicylate can also be used as a transfer agent, to produce a manual copy of an image on a surface.

Historically, soap is sodium (soda ash) or potassium (potash) salt of fatty acids derived by reacting fat with lye in a process known as saponification. The fats are hydrolyzed by the base, Yielding glycerol and crude soap. Soap is a surfactant used in conjunction with water for washing and clearing that historically comes in solid bars but also in the form of a thick liquid. Isoamyl salicylate is also used in cosmetics, like beauty soaps, to give its scent. Saponification is the hydrolysis of an ester under basic conditions to form an alcohal and the sald of the carboxylic acid. Saponification is commonly used to refer to the reaction of the metallic alkali (base) with a fat or oil to form soap. Saponifiable substances are those that can be converted into soap. Sodium hydroxide (NaOH) is a caustic base. If NaOH is used a hard soap is formed whereas when potassium hydroxide (KOH) is used, a soft soap is formed. Vegetable oils and animal fats are fatty esters in the form of triglycerides. Vegetable fats and oils are derived from plants and are composed of triglycerides. Nominally, oils are liquid at room temperature, and fats are solid; a dense brittle fat is called a wax. Although many different parts of plants may yield oil, [20] in commercial practice oil is extracted primarily from the seeds of oilseed plants. The alkali breaks the ester bond and releases the fatty acid and glycerol. If necessary, soaps may be precipitated by salting it out with saturated sodium chloride. The objective of this study was the preparation of isoamyl salicylate by the reaction of isoamyl alcohal and salicylic acid, and then preparation of soap containing the scent of isoamyl salicylate.

2. MATERIALS & METHODS

2A. Experimental Work for the Synthesis of Isoamyl Salicylate

2.1 Method 1 [NaHSO4 as a catalyst]

20 g of salicylic acid were exactly weighed in a round bottom flask. 42 ml of isoamyl alcohol was added into it, along with $NaHSO_4$ as a catalyst. Then the solution was refluxed in rota-mental at 132-135 degree centigrade for 3 hours. No reaction occurred.

2.2 Method 2 [HNO3 as a catalyst]

20 g of salicylic acid were exactly weighted in a round bottom flask. 42 ml of isoamyl alcohol was added into it, along with HNO_3 as a catalyst. Then the solution was refluxed in rotamental at 132-135 degree centigrade for 3 hours. No reaction occurred.

2.3 Method 3 [HCI as a catalyst]

20 g of salicylic acid were exactly weighted in a round bottom flask. 42 ml of isoamyl alcohol was added into it, along with HCI as a catalyst. Then the solution was refluxed in rotamental at 132-135 C for 3 hours. No reaction occurred.

2.4 Method 4 [H_2SO_4 as a catalyst]

20 g of salicylic acid were taken in a round bottom flask. 42 ml of isoamyl alcohol was added into it, along with H_2SO_4 as a catalyst. Then the solution was refluxed in rotamental at 132-135^{o}C for 3 hours. Reaction occured and a clear solution of isoamyl salicylate were prepared.

2B. Experimental work for preparation of beauty soap containing isoamyl salicylate as a scent

2.5 Chemicals required

Pakistani variety of Coconut oil and Almond oil was purchased from Khokhar Oil Traders, Gujranwala-Pakistan. Sodium hydroxide, Boric acid, Ethyl alcohol and n-Hexane were supplied suppliers.

2.6 Method

In a 150 ml beaker following ingredients were added (i) 80 grams of coconut oil (ii) 20 grams of almond oil. In another beaker 17.596 grams of NaOH were dissolved in 41.05733 ml of water. This solution was poured in the beaker containing weighed coconut oil and almond oil. Then a small amount of boric acid was added to it. The two solutions were stirred constantly along the addition of isoamyl salicylate until the soap formed.

2.7 Tests for the analysis of the Beauty soap

2.7.1 pH test

1 g of the prepared smple was taken in 10 ml water. Heated the mixture on a water bath then cooled it. pH was noted with the help of a pH meter.

2.7.2 Volatile moisture content

2 g prepared soap was taken in a petri dish. It was placed in an oven at 102 C for three hour. Then it was cooled in a desicator. The sample was weighed again after drying. Total volatile moisture content can be obtained by following formula:

$$\text{Total volatile moisture conten} = \frac{\text{Wieght after drying}}{\text{Weight before drying}} \times 100$$

2.7.3 Total matter soluble in alcohol

2 g of the prepared soap were taken in a freshly boiled 200 ml ethyl alcohol on a water bath. Sample was dissolved in alcohol. The solution was filtered by the help of an already weighed filter paper, and residues were washed with hot alcohol. Filter paper was dried at 100 C and again was weighed.

2.7.4 Total matter soluble in water

10 g of sample were dissolved in 100 ml of water on a water bath for half hour at 100 C. It was then filtered (already weighed) and dried in an oven and again weighed.

2.7.5 Total fatty matter

5 g of prepared sample of soap were taken and dissolved in a 150 ml of water on a water bath. Heated for 45 mints, and cooled. Solution was taken in a separating funnel. 98 % H_2SO_4 was added drop wise. A fatty layered appeared. It was separated and rinse for two to three times with 80% hexane. Then layer was put in an empty weighed beaker and allowed to evaporate and beaker was weighed again.

2.7.6 Un-sponified matter

5 g sample was taken in a 200 ml flask, and 30 ml of ethyl alcohol was added in it along with a little amount of 50% KOH. It was filtered and water was added till precipitates are formed. It was poured in a separating funnel and 50 ml of hexane was added. It lower layer was taken out and treated with 8 ml of concentrated HCI. Flask was heated and then weighed.

2.7.7 Free fatty matter

5 g sample was taken in a 200 ml flask, and 30 ml of ethyl alcohol was added in it along with a little amount of 50 % KOH. It was foltered and water was added till precipitates are formed. It was poured in a separating funnel and 50 ml of hexane was added. It lower layer was taken out and treated with 8 ml of concentrated HCI. Flask was heated and then weighed.

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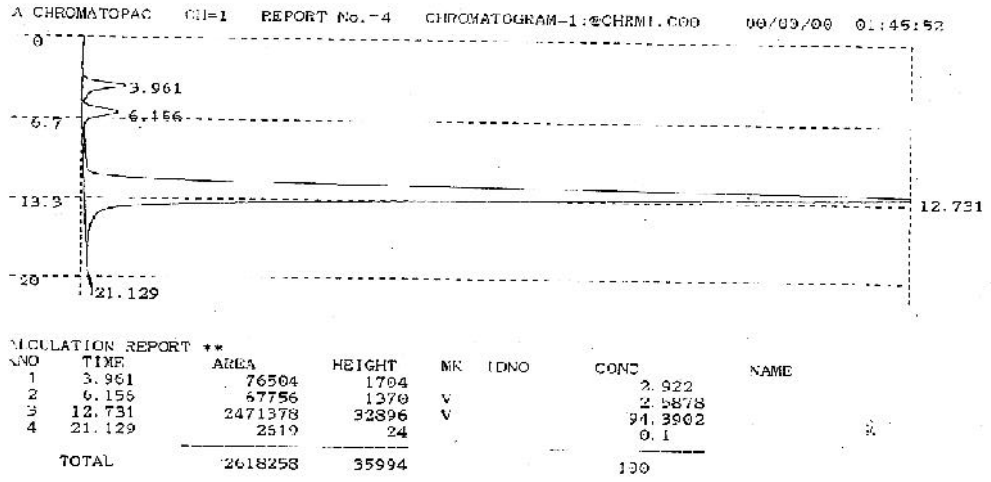

Fig 2 Gas chromatogram Showing 67.71% purity of isoamyl salicylate.

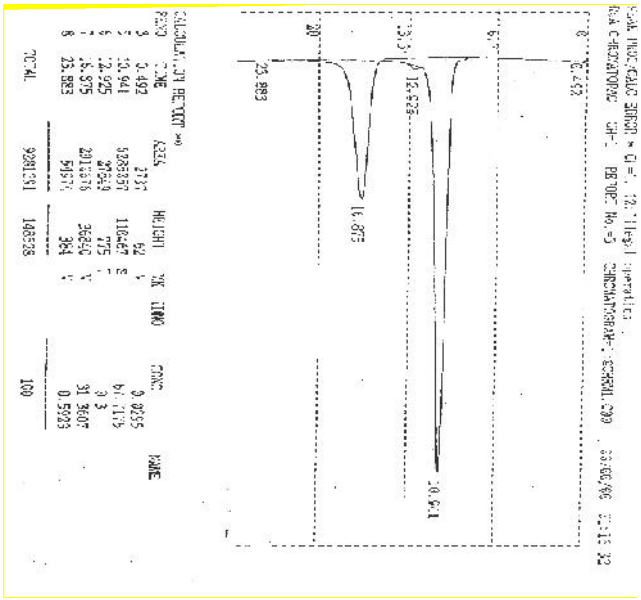

Fig 3 Gas Chromatogram showing 95% yield of isoamyl salicylate

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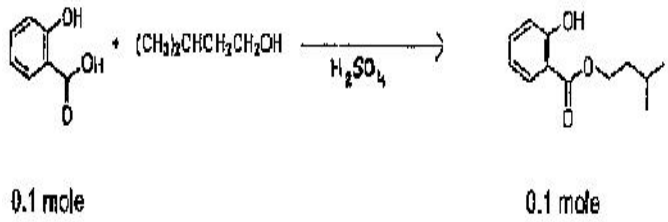
3 RESULTS & DISSCUSSION

3.1 % age yield of isoamyl salicylate



0.1 mole 0.1 mole

20 g of the salicylic acid gives = 26.19 g Isoamyl salicylate
So theoretical yield= 26.19 g
Experimental yield= 24.93 g
% age yield = Experimental yield/ Theoretical yield x 100
= 24.93/26.19 x 100= 95%

Table 1 properties of Isoamyl Salicylate

Visual Description	Clear clolorless liquid
Odor Profile	Herbal, Floral, Green
Olfactory Description	Sweet, soluble, green balsamic blending agent, rounded character.
Molecular Weight	208.22 (g/mol)
Molecular Formula	$C_{12}H_{16}O_3$
H-Bond Donor	1
H-Bond Acceptor	1
Rotatable Bond Count	4
Exact Mass	208.11
Tautomer Count	4
Topological Polar Surface Area	46.5
Heavy Atom Count	15
Refrective index	1.504-1.509
Specific gravity	1.046-1.055

In this research work, "isoamyl salicylate", and "beauty soap" containing fragrance of isoamyl salicylate as a scent were prepared. General methods for the synthesis of "isoamyl salicylate" and preparation of soap are known and raw materials are available in the local market. The aim of present research was to collect literature to synthesize "isoamyl salicylate" on commercial scale in country, as well as preparation of soap containing "isoamyl salicylate". Isoamyl salicylate has a number of applications in cosmetic industry. It is used as a flavoring agent, and to provide fragrance to various products.

The research work was invented to synthesize the isoamyl salicylate by using the H_2SO_4 as a catalyst, "isoamyl salicylate" by this using H_2SO_4 as a catalyst gave high yield 95%, but with product purity of 67.7175%. Tingshum Jianga et al. (2008) used the salicylic acid and isoamyl alcohol for ester formation, and tested the catalytic activities of the catalysts. Prepared solid super acid, conventional liquid acid H_2SO_4 and Mesoporous TiO_2 were tested under the same experimental conditions. The results showed that the catalytic activities of the prepared solid super acid catalysts were higher than that of the conventional liquid acid H_2SO_4, and that the catalytic activity of mesoporous TiO_2 solid super acid is the highest among the three catalysts [21]. Chitralekha Khatria, and ashu Rani, (2008) synthesized nano-crystalline activated fly ash catalyst (AFAC) with crystallite size of 12 nm. Result was a very high conversion 87% of salicylic acid to methylsalicylat (oil of Wintergreen), and 81% of salicylic acid to isoamyl salicylate [22].

The other catalysts were also used like $NaHSO_4$, HNO_3, and HCI, to obtain high product purity. But isoamyl salicylate was prepared only when H_2SO_4 was used as a catalyst. In this method salicylic acid and isoamyl alcohol are reacted to each other, in the presence of sulfuric acid as a catalyst. The product purity was 67.7175% as shown by fig 2 and total yield was 95% as shown in fig 3. The boiling point of the prepared solution of the isoamyl salicylate was 276.4^{o}C. The melting point of prepared "isoamyl salicylate" was 276.3^{o}C. Our results were acceptable and promising and objectives were achieved.

The purity of the "isoamyl salicylate" was determined by the help of "Gas Liquid chromatography (GLC)". The purity of the prepared sample was 67.7175%. GLC is an authentic technique, and confirmed the purity of prepared compound. Villa C. et al, (2007) worked to quantify 24 volatile perfumery chemicals including isoamyl salicylate. The 24 analytes were appropriately separated out for a running time of 40 min, on a C18 column using a simple gradient elution (acetonitrile/water) with flow rate from 0.7 to 1.0 ml/min and UV acquisition at 210, 254 and 280 nm. All calibration curves showed good linearity (r2 > 0.99) within test ranges. The method was successfully applied to the qualitative and quantitative determination of the potential allergens in four commercial scented, with satisfactory accuracy and precision [23]. G. Kuriakose and N. Nagaraju, (2004) Showed a systematic study to find the effect of amount of the catalyst, the molar ratio of alcohol to salicylic acid and the duration of reaction on the synthesis of the ester. They used Al203, SiO2, ZrO2 and their sulfated forms. Products obtained were analyzed on gas chromatograph and further characterized by GC-MS, IR, NMR and 13C NMR. All the catalysts were found to be active and exhibit 100% Selectivity towards the formation of esters [24]. Our results are better due to high yield and cost effectiveness.

The prepared "isoamyl salicylate" was then used as a fragrance in the preparation of "beauty soap". Beauty soap containing the fragrance of isoamyl salicylate as a scent was prepared and analyzed by the help of seven tests.

The pH of the soap was detected by using an appropriate method, was 10. Amount of volatile moisture content was 0.955%. Total matter insoluble in alcohol was 1.55%. Total matter soluble in water was calculated to be 0.1 g. Total fatty matter soluble in water was 1.1 %. Amount of un-sponified matter, was obtaine to 96.2%. Amount of free fatty matter was obtained to 63%.

4 CONCLUSIONS

Although the work has been carried out on the synthesis of isoamyl salicylate in different countries, but it has not been thoroughly studied in Pakistan. The present study of the isoamyl salicylate indicates that it has many industrial applications, especially in cosmetic industry. Further

investigation is required to obtain high purity of isoamyl salicylate. The indigenous production of isoamyl salicylate and "beauty soap" will save a lot of foreign exchange. It will increase the well trained & skilled man power.

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6 REFERENCES

1. Salicylic acid. The *Columbia Encyclopedia*, **6**th Ed., (2008)
2. Kirk-Othmer Encyclopedia of Chemical Technology. New York: Wiley, (1991)
3. Frosch P., Johansen J. D., White I. R., Fragrances, Beneficial and adverse Effects. *1st Ed. Springer*, (1998)
4. Bauer K., Garbe D., Surburg H., Common Fragrance and Flavor Meterials. **2nd**, revised edition ed. jointly by VCH Verlagsgesellschaft,
5. de Groot A. C., Frosch P. J., Adverse reactions to fragrances, A clinical review. *Content Dermatitis Feburary*, **36**(2):57-86 (1997)
6. Jensen O. C., Petersen I., Occupational asthma caused by scented gravel in cat litter boxes. *Ugeskr leager*; **153**(13):939-40 (1991).
7. Lessenger JE., Occupational acute anaphylactic reaction to assault by perfume spray in the face. *J Am Board Fam Pract*., **14**(2):137-40(2001)
8. Wray D, Rees SR, Gibson J, Forsyth A.,The role of allergy in oral mucosal diseases. QJM **93**(8):507-11 (2000).
9. Nielsen NH, Linneberg A, Menne T, Madsen F, Frolund L, Dirksen A., Allergic contact sensitization in an adult Danish population: two cross- sectional surveys eight years apart (the Copenhagen Allergy Study). *Acta Derm Venereol* ;**81**(1):31-4 (2001)
10. Schnuch A, Uter W, Geier J, Gefeller O., Epidemiology of contact allergy: an estimation of morbidity employing the clinical epidemiology and drug-utilization research (CE-DUR) approach. *Contact Darmatitis*; **47**(1):32-9 (2002)
11. Frosch PJ, Johansen JD, Menne T, Pirker C, Rastogi SC, Andersen K. E., Further important sensitizers in patients sensitive to fragrances. *Contact Dermatitis*, **47**(2):78-85 (2002)
12. Baur X, Schneider EM, Wieners D, Czuppon A. B., Occupational asthma to perfume. *Allergy*, **54**(12):1334-5 (1999).
13. Millqvist E, Lowhagen O., Placebo-controlled challenges with perfume in patients with asthma-like symptoms. *Allergy*, **51**(6):434-9 (1996)
14. Millqvist E, Bende M, Lowhagen O., Sensory hyperreactivity - a possible mechanism underlying cough and asthma-like symptoms, *Allergy* **53**(12):1208-12 (1998).
15. James G. D., Price S. T., "Field-testing of isoamyll salicylate for recruitment and retention of beneficial insects in grapes and hops", *J. Chem. Ecol*. **30** (8): 1623-28 (2004)
16. Shulaev V., Silverman P., Raskin I., Airborn signalling by isoamyl salicylate in plant pathogen resistance, *Nature* **385**, 718-721 (1997)
17. Norman S., The Formula Book, New York: Sheed and Ward, **28** (1975)
18. Schiestl, F.P., Roubik, D.W.. Odor Compound Detection in Male Euglossine Bees, *J. Chem. Ecol*. **29**: 253-257 (2011)
19. Harvey E. N., The luminescence of suger wafers, *Sci. mag*., Vol. **90**. No.2324, 35-36 (1939)
20. Filippa M., Sancho M. I., Gasull E., Encapsulation of methyl and ethyl salicylates by beta-cyclodextrin HPLC, UV-vis and molecular modeling studies. *Pharm Biomed Anal*. **36** (9) 342-349 (2010)
21. Tingshun Jianga, Qian Zhao, a, , Mei Lia and Hengbo Yina. *Journal of Hazardous Materials* (2008).
22. Chitralekha Khatria, and ashu Rani A. *Fuel*, Vol. **87**, 2886-2892 (2008)
23. Villa C., *J. Pharma. Biomed. Analysis* Vol. **44**, 755-762 (2007)
24. Kuriakos G. Nagaraju N., *Journal of Molecular Catalysis, Chemical* Vol. **22 3**, 155-159 (2004)