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Novel and Simple Gas Chromatographic Method for the Quantification of Schiff Base Compounds

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ABSTRACT: *An accurate, simple, novel and advancedmethod of quantifying Schiff's bases was developed and reported by GC. N-Benzyl aniline, N-Salicylide-aniline and N-(-4-Methoxy benzylidene) aniline were selected as the target compounds and the underlying method can quantify thesecompounds over a wide range of 10 ppm to 2000ppm. GC instrument equipped with flame ionization detector was selected for the assay based on the physic chemical properties of the compounds*.

Keywords: N-Benzyl aniline, N-Salicylide-aniline and N-(-4-Methoxy benzylidene) aniline, Gas chromatography, Capillary column, HP-5 MS.

INTRODUCTION:

Recently owing to the drastic environmental impact of the chemicals, solvents and reagents, an alternative way of chemistry was designed and used by many chemists worldwide. The most generous term for this eco-friendly and less toxic approach is the Green chemistry approach and it is being used for the synthesis ofvarious organic compounds and key intermediates in recent past [1]. This technique involves an alternative reaction media to replace hazardous and expensive solvents routinely used in organicsynthesis laboratories [2-4]. Few approaches of using fruit juices as potential organic solvents for the synthesis of various naturally derived compounds of pharmaceutical interest were reported [5]. Researchers worldwide are interested in applications of different fruit juices due to their nontoxic, safe, inexpensive and environmentally benign nature [6]. Fruit juice is being used onregular basis in various organic transformation reactions [7-10]. Lemon juice is themost familiar fruit juice employed in different important organic reactions like Knoevenagel condensation reaction [11],synthesis of triazoles [12] and synthesis of Dihydropyrimidinone [13] and many more such reactions. Schiff's bases are important member of organic compounds and they possesses varieties of biological activities such as anticancer [14], antibacterial [15,16] anti-fungal [17] properties. Schiff's bases can be synthesizedinmanyways[18,19]. So far, so many environmental friendly, solvent free and metal catalyzed reactions were reported [20-22]. However,

these methods have number of limitations pertaining to environmental pollution, cost effectiveness, low yield of products. The current study based on String technique is proven to fasten the reaction rate, improved yields and uses low energy input[23]. Mechanism involves in String reactions is cavitation, a type of physical force producing growth, oscillation, and bubble collapse inside the reaction [24]. Present work reports the synthesis of classical Schiff's base using Different berry fruit juice freeze dry powder as a green catalyst. Schiff's base was synthesized by conventional as well as string methods in order to compare percentage yield, reaction time,and assay,In this proposed method gas chromatography equipped with flame ionization detector was used. HP-5MS capillary column was the stationary phase. The method produced faster,specific, repeatableand robust results.

Materials and methods:

2.1 Apparatus:

Instrument : GC – 2010 Plus (Shimadzu) or any other equivalent

2.2 Chromatographic conditions:

Column : HP-5 MS or any other equivalent

Length : 30 mtrs

Diameter : 0.25 mm

Film thickness : 0.25µm

Detector : FID

Carrier gas : Nitrogen

Nitrogen flow rate : 1.0 ml/minute

Hydrogen flow rate : 40 ml/minute

Air : 400 ml/minute

Split ratio : 1:50

Injection volume : 1 µl

Flow rate : 1.0 ml/ minute

Diluent :Ethyl acetate (GC grade or any equivalent).

Temperature program :

Rate, per minute	Column temperature	Hold time, Minutes
-	150°C	0
15°C	300°C	2

Injector temperature : 180°C

Detector temperature : 300°C

Total run time : 12.0 minutes

Retention time for N-Benzyl aniline : About 4.5 minutes

Retention time for N-Salicylide aniline : About 5.5 minutes

Retention time for N-(4-methoxy benzylidene) aniline: About 6.3 minutes

3.0 PROCEDURE:

Diluent : Ethyl acetate (GC grade or any other equivalent).

Standard preparation:

10 mg each of N-Benzyl aniline, N-Salicylide-aniline and N-(-4-Methoxy benzylidene) aniline standardswere weighed accurately into a 10 ml clean and dried volumetric flask, 5 ml of Ethyl acetate was added and the flask was sonicated for 5 minutes. Cooled to room temperature and the volume was made up to the mark with Ethyl acetate. The contents were mixed well by shaking the flask.

Sample preparation:

Synthesis of Schiff's base via string Method.

Anisaldehyde or Benzaldehyde or Salicylaldehyde can be used as a starting material. For the ease of sourcing and handling Anisaldehyde was chosen for the present study. Anisaldehyde (0.01 mole) and Aniline (0.01 mole) were taken in equal amounts in a conical flask and 4mL of 1% solution of individual Mango fruit juice freeze dry powder in methanol was added to the flask drop wise over a period of 2 min.Similarly, solutions were prepared with Pomegranate fruit, Sweet lemon fruit, Jamun fruit, Acai berry fruit, Goji berry fruit, Macqui berry fruit and Black berry fruit juice freeze dried extracts. A mixture of different fruit juices was also evaluated. The contents of the flask were stirred at about 500rpm for 25 minutes at room temperature.After 25 min the completion of the reaction was confirmed by TLC (Mobile phase:-n-hexane:Ethyl acetate ::80:20, Plate:- Silica). Triplicate preparations were made to ensure the authentication of theprocess. Recrystallization with ethyl acetate resulted in a crystalline compound which was subsequently characterized.

10 mg each of the inhouse-produced N-Benzyl aniline, N-Salicylide-aniline and N-(-4-Methoxy benzylidene) aniline samples were weighed accurately into a 10 ml clean and dried volumetric flask, 5 ml of Ethyl acetate was added and the flask was sonicated for 5 minutes. Cooled to room temperature and the volume was made up to the mark with Ethyl acetate. The contents were mixed well by shaking the flask.

System suitability procedure:

Injected the diluent as blank until a stable baseline was achieved. Injected the standard and again injected the blank to check the carryover.

Standard was injected 6times and the % RSD for standard area was checked.

Relative standard deviation (%RSD) : NMT 2.0%

Theoretical plates : NLT 5000

Tailing factor : NMT 2.0

Sample analysis was continued once the stated system suitability parameters were achieved.

Procedure for sample analysis:

1µl of the sample solutions were injected in duplicate and correspondingpeaks from the standard chromatogram were integrated and average sample area from duplicate injections was considered for calculation.

Calculation:

A1 W2 10

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$$\text{N-Benzyl aniline content, \% w/w} = \frac{A1}{A2} \times \frac{10}{W1} \times \text{\% Purity}$$

N-Benzyl aniline content, in ppm = N-Benzyl aniline content, % w/w X 10000

$$\text{N-Salicylide-aniline content, \% w/w} = \frac{A1}{A2} \times \frac{W2}{10} \times \frac{10}{W1} \times \text{\% Purity}$$

N-Salicylide-aniline content, in ppm = N-Salicylide-aniline content, % w/w X 10000

$$\text{N-(-4-Methoxy benzylidene) anilinecontent, \% w/w} = \frac{A1}{A2} \times \frac{W2}{10} \times \frac{10}{W1} \times \text{\% Purity}$$

N-(-4-Methoxy benzylidene) aniline content,
in ppm = N-(-4-Methoxy benzylidene) anilinecontent, % w/w X 10000

Where,
A1 = Average area of sample peak corresponding to standard peak
A2= Average area of standard peak
W1= Weight of sample in gram
W2=Weight of standard in gram
P= % purity of standard

3 EXPERIMENTAL RESULTS& DISCUSSION:

GC was chosen as the preferred instrument for the assay. Several combinations of columns and temperature programs were evaluated before finalizing the method parameters. Validation of the method was performed as per ICH guidelines for specificity, precision, linearity, robustness, detection limit, quantification limit and accuracy and the method stands to be validated. Limit of detection and limit of quantification were determined to be 0.1ppm and 0.5ppm respectively.

3.1 Repeatability and reproducibility.

The repeatability and reproducibility of the analytical method were demonstrated from the peak area and retention times of the standard solution. The results as listed in Table 1,& Fig 1, indicated acceptable repeatability and precision (RSD<2%).

Table-1: Repeatability and reproducibility of the peak area of standard solution (*n*=6) by GC

Sl,No	N-Benzyl aniline	N-Salicylide-aniline	N-(-4-Methoxy benzylidene) aniline
1	431553	417749	407101
2	429533	417020	405877
3	428098	415592	404976
4	432130	419640	409278
5	431165	418469	407184
6	433543	422215	412171
Avg	431003.666	418447.500	407764.500
SDEV	1931.341	2293.299	2600.904
% RSD	0.448	0.548	0.637
Tailing factor	1.112	1.041	1.100
Theoretical plates	200629	265334	319580

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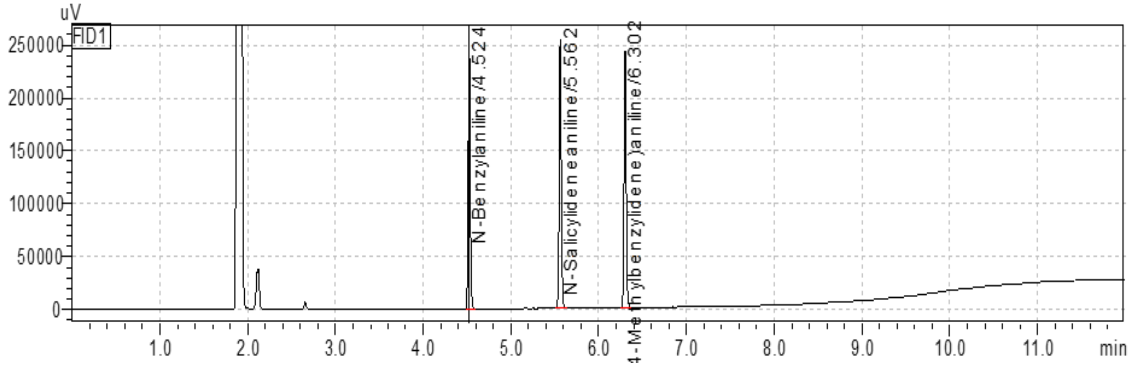
Fig, 1. Representative chromatogram:
Standard.



3.2 Assay of Schiff's base compounds:

The assay results of the N-Benzyl aniline, N-Salicylide-aniline and N-(-4-Methoxy benzylidene) anilineof different Berry fruit juice freeze dry powder were reported in Table 2. The assay results represent acceptable recovery levels across the evaluated berry fruit juice freeze dried extracts.

Table 2: Assay of the N-Benzyl aniline, N-Salicylide-aniline and N-(-4-Methoxy benzylidene) aniline.

Sl.No	Compound Name	Assay determined by GC		
		N-Benzyl aniline	N-Salicylide-aniline	N-(-4-Methoxy benzylidene) aniline
1	0.01 Molar sulfuric acid	92.65 %	98.23 %	97.25 %
2	0.1 % Gallic acid	98.94 %	98.22 %	96.89 %
3	Mango fruit juice freeze dry powder (1% Methanolic solution)	97.80 %	100.06 %	99.69 %
4	Pomegranate fruit juice freeze dry powder (1% Methanolic solution)	99.68 %	100.18 %	98.21 %
5	Sweet lemon fruit juice freeze dry powder (1% Methanolic solution)	98.72 %	100.29 %	98.15 %
6	Jamun fruit juice freeze dry powder (1% Methanolic solution)	97.98 %	98.54 %	99.33 %
7	Acai berry fruit juice freeze dry powder (1% Methanolic solution)	99.62 %	99.47 %	98.33 %
8	Goji berry fruit juice freeze dry powder (1% Methanolic solution)	100.57 %	103.11 %	96.93 %
9	Black berry fruit juice freeze dry powder (1% Methanolic solution)	100.17 %	99.24 %	97.45 %
10	Macqui berry fruit juice freeze dry powder (1% Methanolic solution)	100.52 %	100.33 %	98.93 %
11	3 to 6 mix berry fruit juice freeze dry powder (1% Methanolic solution)	98.25 %	100.28 %	100.13 %
12	7 to 10 mix berry fruit juice freeze dry powder (1% Methanolic solution)	100.12 %	100.45 %	99.47 %

Each value is mean±Std.Dev. of duplicate analysis.

4. CONCLUSION:

The stated analytical method for the quantification of Schiff's bases by GCstands to be validated as per ICH. The method is specific, selective, linear, accurate, precise and robust. Rapid quantification was achievedby optimizing some method parameters and the current optimized can quantify the Schiff's bases faster than the published methods. This method stands suitable for the quantification of N-Benzyl aniline, N-Salicylide-aniline and N-(-4-Methoxy benzylidene) aniline.

5. Data availability statement:-

The data used to support the findings of this study are included within the article. For further information, the primary author can be contacted on the provided email address.

6. Funding statement:-

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7. Conflict of interest:-

The authors declare that there is no conflict of interest regarding the publication of this paper.

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