DEVELOPMENT AND VALIDATION OF A GAS CHROMATOGRAPHY HEADSPACE METHOD FOR THE SIMULTANEOUS QUANTIFICATION OF SIX ORGANIC VOLATILE IMPURITIES IN SUMATRIPTAN SUCINATE API AND ITS PHARMACEUTICAL DOSAGE FORMS

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Received: 24 February 2020, Revised and Accepted: 22 April 2020

INTRODUCTION

Sumatriptan succinate (Fig. 1) is chemically 3-[2-(dimethylamino)ethyl]-N-methyl-indole-5-methanesulfonyamide succinate [1]. Chemical formula is C_{18}H_{27}N_{3}O_{5}S and molecular weight is 413.5 g/mol.

Organic volatile chemicals used in synthesis and process chemistry of drug substances. There is an existing International Conference on Harmonization (ICH) guideline for residual solvents in pharmaceuticals (ICH 1997).

LITERATURE REVIEW

A literature survey regarding the quantitative analysis of sumatriptan succinate revealed that attempts were made to the estimation of sumatriptan succinate in bulk and pharmaceutical dosage forms by high-performance liquid chromatography (HPLC) [1,2] and simultaneous estimation of sumatriptan succinate, metoclopramide hydrochloride, and paracetamol by reverse-phase HPLC [3].

In this study, methanol, acetone, isopropyl alcohol (IPA), dichloromethane, benzene, and toluene were taken as a volatile organic impurity (Fig. 2). The specifications for the six organic volatile impurities were taken very low level compared with ICH specifications. The results obtained were validated according to the ICH guidelines.

METHODS

Chemicals and reagents

Methanol (HPLC grade), acetone (HPLC grade), IPA (HPLC grade), dichloromethane (gas chromatography [GC] grade), benzene (HPLC grade), toluene (HPLC grade), and dimethyl sulfoxide (DMSO) (GC grade) were provided by Sigma-Aldrich. Sumatriptan succinate active pharmaceutical ingredients (API) are taken from a local research laboratory. DMSO is used as a diluent and blank.

Apparatus and chromatographic conditions

Chromatography was performed on a Shimadzu chromatographic system equipped with a Shimadzu GC-2010 system with a flame ionization detector (FID), samples were injected through a Teledyne Tekmar HT3™ Headspace (HS). Data acquisition and integration were performed using GC solution software. The instrument parameters described below were set up to determine the organic volatile impurities.

GC conditions

The column was DB-624 3.0 μm film thickness, 30 m, and 0.53 mm. The column flow is 2.8 mL/min injector temperature: 220°C. The detector temperature is 260°C. The oven temperature is 260°C. The oven program is, initial temperature is 40°C hold for 12 min. The split ratio is 20:1 and the carrier gas is N_{2}.

HS conditions

Vial temperature is 90°C, oven temperature is 100°C, transfer line temperature is 110°C, vial equilibration time is 25 min, inject time is 1.0 min, and GC cycle time is 35 min.

Preparation of solutions

Specifications for organic volatile impurities

Methanol is 2000 ppm, acetone is 1000 ppm, IPA is 500 ppm, dichloromethane is 500 ppm, benzene is 2.0 ppm, and toluene is 500 ppm.

RESULTS

The correlation coefficient (r²) was not <0.99 at the limit of quantification (LOQ) to 150%. The limit of detection obtained for methanol, acetone, isopropyl alcohol, dichloromethane, benzene, and toluene was found 18.4, 8.8, 5.5, 4.3, 0.04, and 4.2 ppm. The LOQ obtained was 55.8, 26.8, 16.6, 13.0, 0.1, and 12.6 ppm. Accuracy results were obtained from 85 to 115% for six OVI’s. Furthermore, verified precision, ruggedness, robustness, solution stability, and pharmaceutical analysis. All the results are found within the acceptable limits.

Conclusion:

The method presents a simple and reliable solution for the routine quantitative analysis of organic volatile impurities present in sumatriptan succinate API.

Keywords: Methanol, Acetone, Isopropyl alcohol, Dichloromethane, Benzene, Toluene, Sumatriptan Succinate active pharmaceutical ingredients, Method development and Validation.

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**Benzene standard stock solution**
Weigh and transferred about 250 mg of benzene into a 50 mL of the volumetric flask containing 30 mL of diluent and diluted to volume with diluent. Further taken 1.0 mL of above solution into 100 mL of volumetric flask and diluted to volume with diluent.

**Standard solution preparation**
Weigh and transferred about each 500 mg of methanol, 250 mg of acetone, 125 mg of IPA, 125 mg of dichloromethane, and 125 mg of toluene into a 100 mL of the volumetric flask containing 70 mL of diluent and diluted to volume with diluent. Further taken 5.0 mL of the above solution and 0.5 mL of benzene stock solution into 50 mL of volumetric flask and diluted to volume with diluent.

The standard HS vials were prepared with 2 mL of the standard solution and seal the vial with aluminum closure (the standard solution concentration was prepared concerning sample concentration).

**Preparation of sumatriptan succinate API sample solution (250 mg/mL)**
Accurately weighed about 500 mg of sumatriptan succinate API into an HS vial and add 2.0 mL of DMSO was accurately pipetted into the sample vial. The vial was sealed with aluminum closure.

**Preparation of sumatriptan succinate tablet solution**
Twenty tablets were weighed and powdered. An amount of powder equivalent to 500 mg sumatriptan succinate was accurately weighed and transferred to an HS vial, add 2 mL of diluent and seal with an aluminum septum and crimp the cap.

**Calculation**
The organic volatile impurity content was calculated from,

\[
PPM(OVI) = \left(\frac{\text{Impurity area in API Concentration}}{\text{Impurity area in Standard solution Concentration}}\right) \times 10^6
\]

**RESULTS AND DISCUSSION**

**Method development**
The GC-HS method has been developed as stepwise strategies.

**Column selection**
The primary goal of column selection was to resolve a total of six organic volatile impurities which were used during the synthesis and manufacturing of sumatriptan succinate API. Several columns were initially investigated to finalize a single column for the separation and quantitation of organic volatile impurities. Wall-coated capillary columns of various brands with a variety of phases and dimensions have been investigated. The 1st column is DB-1 (30 m length, 0.32 mm i.d, 1.0 µ film thickness). The 2nd column is VF-624 ms (60 m length, 0.32 mm i.d, 1.0 µ film thickness). Moreover, the 3rd column is DB-624 (30 m length, 0.32 mm i.d, 3.0 µ film thickness). In the above the 1st and 2nd columns, the response was found to be comparatively lower and peak shapes were found to be unsatisfactory, and the resolution is not good. However, the 3rd column has given good resolution, tailing, and good peak shapes. Therefore, DB-624 (30 m length, 0.53 mm i.d, 3.0 µ film thickness) proved to be the best column that could fulfill all the needs of the method, those are higher sensitivity, shorter runtime, and higher resolution between the critical pairs.

**HS method optimization**
The HS method was optimized in such a way that the maximum amount of the organic volatile impurities present in the sumatriptan succinate API gets evaporated for the detection. For this, the standard and sample vials were heated at 70°C-100°C for 15-30 min with constant shaking. A combination of sample vial heating at 90°C with 25 min shaking was found to be suitable for getting a good response.

**Method validation**
The developed GC-HS method has been validated as per ICH guideline [4].

**Specificity**
The relative retention time of the six OVI's indicated that they were well separated from each other (Table 1). The typical chromatograms of six organic volatile impurities and sumatriptan succinate API is shown in Fig. 3.

**System suitability**
System suitability was evaluated by injecting six replicates of standard solution into the chromatographic system as per the test method. The % relative standard deviation (RSD) was calculated for the area of six OVI’s. The % RSD of each impurity is not more than (NMT) 15.0%. Results and typical chromatograms are shown in Table 2 and Fig. 4.

**Method precision**
Method precision was evaluated by preparing the six different preparations of standard solution into the chromatographic system as per the test method, % RSD was calculated for area of six preparations. The % RSD of each organic volatile impurity is NMT 15.0%. Results and typical chromatograms are shown in Tables 3 and Fig. 5.

**Linearity at low level for limit of detection (LOD) and limit of quantification (LOQ)**
The linearity of the method was determined over the concentration range of 5%, 10%, 15%, 20%, and 25% concerning the sumatriptan succinate API. The LOD and LOQ were calculated from these linearity data and shown in Table 4.

**LOD and LOQ**
The LOD and LOQ for the proposed method were determined using calibration standards and calculated using 3.3 s/s and 10 s/s formulae, respectively. The data and typical chromatograms are as shown in Table 5 and Fig. 6.

**Linearity with LOQ**
The linearity of the method was determined over the concentration range of LOQ %, 50%, 75%, 100%, 125%, and 150%. The correlation coefficient (r²) of each impurity is not <0.99. The obtained results and typical chromatograms for linearity as shown in Table 6 and Fig. 7.

**LOQ-precision**
The % RSD of the area obtained from six standard injections at LOQ level was calculated. The % RSD is abstained NMT 15.0%. The obtained results and typical chromatograms for LOQ precision as shown in Table 7 and Fig. 8.

**Accuracy**
The accuracy was evaluated by the % recoveries of the six organic volatile impurities spiked with the sumatriptan succinate sample API. The acceptance criterion for accuracy was that should be in the range of 85-115%. The results are indicated in Table 8.

**LOQ accuracy**
The % recovery of each organic volatile impurity at the LOQ level should be within 100±15%. The results are shown in Table 9.
Fig. 2: Chemical structures of six organic volatile impurities

- Methanol
  Chemical Formula: CH₃OH
- Acetone
  Chemical Formula: C₃H₆O
- Isopropyl alcohol
  Chemical Formula: C₃H₈O
- Dichloromethane
  Chemical Formula: CH₂Cl₂
- Benzene
  Chemical Formula: C₆H₆
- Toluene
  Chemical Formula: C₇H₈

Fig. 3: Typical chromatograms of six organic volatile impurities standard and sumatriptan succinate

Fig. 4: Typical chromatogram for system suitability
Fig. 5: Typical chromatogram for method precision

Fig. 6: (a) Limit of detection and (b) limit of quantitation chromatogram of six organic volatile impurities

Fig. 7: Linearity with a limit of quantitation graphs of six organic volatile impurities
Table 1: Specificity data for six organic volatile impurities

| S. no. | Name of OVI's | RT (min) | Theoretical plates | Tailing factor | USP resolution |
|--------|---------------|----------|--------------------|----------------|----------------|
| 1.     | Methanol      | 3.84     | 31,500             | 1.24           | --             |
| 2.     | Acetone       | 5.88     | 31,592             | 1.25           | 18.81          |
| 3.     | IPA           | 6.15     | 31,670             | 1.24           | 2.00           |
| 4.     | MDC           | 6.62     | 31,378             | 1.25           | 3.63           |
| 5.     | Benzene       | 9.49     | 31,895             | 1.23           | 24.58          |
| 6.     | Toluene       | 11.53    | 31,437             | 1.25           | 19.28          |

OVI's: Organic volatile impurities, IPA: Isopropyl alcohol, MDC: Methylene dichloride, USP: United States pharmacopeia

Table 2: System suitability data for six organic volatile impurities

| No. of injections | Area of methanol | Area of acetone | Area of IPA | Area of MDC | Area of benzene | Area of toluene |
|------------------|------------------|----------------|-------------|-------------|----------------|----------------|
| 1.               | 419,110          | 836,915        | 157,745     | 93,538      | 2588           | 498,177        |
| 2.               | 387,746          | 855,404        | 169,561     | 96,748      | 2702           | 519,538        |
| 3.               | 437,461          | 866,166        | 191,123     | 103,363     | 2900           | 584,455        |
| 4.               | 414,158          | 866,780        | 161,318     | 96,789      | 2654           | 506,330        |
| 5.               | 494,852          | 901,815        | 191,230     | 103,363     | 2702           | 527,798        |
| 6.               | 431,293          | 961,979        | 230,239     | 103,363     | 2900           | 522,898        |

Table 3: Method precision data for six organic volatile impurities

| No. of injections | Area of methanol | Area of acetone | Area of IPA | Area of MDC | Area of benzene | Area of toluene |
|------------------|------------------|----------------|-------------|-------------|----------------|----------------|
| 1.               | 549,752          | 865,575        | 152,638     | 97,377      | 2648           | 513,474        |
| 2.               | 583,141          | 803,999        | 162,296     | 100,231     | 2720           | 541,205        |
| 3.               | 628,288          | 899,525        | 177,205     | 103,111     | 2962           | 566,302        |
| 4.               | 594,609          | 884,003        | 166,781     | 99,914      | 2827           | 538,721        |
| 5.               | 742,800          | 937,860        | 209,196     | 109,668     | 3050           | 625,924        |
| 6.               | 650,688          | 893,877        | 184,865     | 102,103     | 2847           | 561,709        |
| AVG.             | 624,880          | 894,138        | 175,617     | 102,103     | 2847           | 557,889        |
| STDV.            | 94.8             | 2.48           | 10.68       | 3.52        | 4.07           | 6.16           |

Table 4: Low-level linearity data for LOD and LOQ

| Con. (%) | Methanol average area (n=2) | Acetone average area (n=2) | IPA average area (n=2) | MDC average area (n=2) | Benzene average area (n=2) | Toluene average area (n=2) |
|----------|-----------------------------|-----------------------------|------------------------|------------------------|--------------------------|---------------------------|
| 5        | 18,784                      | 40,776                      | 7099                   | 4796                   | 115                      | 26,659                    |
| 10       | 40,563                      | 85,649                      | 15,676                 | 10,151                 | 238                      | 53,845                    |
| 15       | 59,479                      | 121,965                     | 23,446                 | 14,456                 | 358                      | 76,261                    |
| 20       | 78,221                      | 165,878                     | 30,454                 | 19,422                 | 481                      | 100,954                   |
| 25       | 97,106                      | 208,443                     | 38,007                 | 24,346                 | 646                      | 126,971                   |
| r²       | 1.000                       | 1.000                       | 0.999                  | 1.000                  | 0.998                    | 1.000                     |
| STEYX    | 1084                        | 2223                        | 508                    | 250                    | 16                       | 1242                      |
| SLOPE    | 3886                        | 8311                        | 1531                   | 967                    | 26                       | 4955                      |
| LOD (%)  | 0.92                        | 0.88                        | 1.10                   | 0.85                   | 2.01                     | 0.83                      |

Table 5: LOD and LOQ data for six organic volatile impurities

| OVI's     | LOD con. (ppm) | LOQ con. (ppm) | LOD area | LOQ area |
|-----------|----------------|----------------|----------|----------|
| Methanol  | 18.4           | 55.8           | 3607     | 10,564   |
| Acetone   | 8.8            | 26.8           | 7803     | 22,175   |
| IPA       | 5.5            | 16.6           | 1628     | 4697     |
| MDC       | 4.3            | 13.0           | 921      | 2654     |
| Benzene   | 0.04           | 0.1            | 52       | 149      |
| Toluene   | 4.2            | 12.6           | 2788     | 13,232   |

LOD: Limit of detection, LOQ: Limit of quantitation, IPA: Isopropyl alcohol, MDC: Methylene dichloride

Ruggedness

The ruggedness of the method was evaluated by performing the sample analysis in six replicates by different analysts on different days and the results are summarized as shown in Table 10. The % RSD values of six organic volatile impurities are NMT 15.0%.

Robustness

This study was performed by making small variations in the method parameters. The variation in the column flow 2.5 mL/min and 3.1 mL/min, vial condition temperature 75°C and 85°C was done. The obtained % RSD is not more than 15% for every changed method parameter. The results are shown in Table 11.
Fig. 8: Limit of quantitation-precision overlay chromatogram for six organic volatile impurities

Fig. 9: Typical chromatogram for sumatriptan succinate tablet

Table 6: Linearity data with LOQ

| Con. (%) | Methanol average area (n=2) | Acetone average area (n=2) | IPA average area (n=2) | MDC average area (n=2) | Benzene average area (n=2) | Toluene average area (n=2) |
|---------|-----------------------------|-----------------------------|------------------------|------------------------|---------------------------|---------------------------|
| *LOQ    | 10,564                      | 22,175                      | 4697                   | 2654                   | 149                       | 13,232                    |
| 50      | 216,607                     | 428,312                     | 79,477                 | 51,182                 | 1459                      | 261,796                   |
| 75      | 320,383                     | 651,986                     | 121,310                | 76,085                 | 2088                      | 400,712                   |
| 100     | 424,672                     | 868,749                     | 164,318                | 98,650                 | 2702                      | 529,494                   |
| 125     | 573,707                     | 1,112,533                   | 221,250                | 126,748                | 3458                      | 702,502                   |
| 150     | 689,391                     | 1,323,137                   | 269,995                | 150,249                | 4189                      | 832,121                   |
| r²      | 0.999                       | 1.000                       | 0.998                  | 1.000                  | 0.999                     | 0.999                     |

*LOQ (%): 2.79% for methanol, 2.68% for acetone, 3.32% for IPA, 2.59% for MDC, 6.09% for benzene and 2.51% for toluene. LOD: Limit of detection, LOQ: Limit of quantitation, IPA: Isopropyl alcohol, MDC: Methylene dichloride

Table 7: LOQ-precision data

| No. of injections | Area of methanol | Area of acetone | Area of IPA | Area of MDC | Area of benzene | Area of toluene |
|-------------------|------------------|-----------------|-------------|-------------|----------------|----------------|
| Run-1             | 10441            | 22071           | 4752        | 2609        | 152            | 12865          |
| Run-2             | 9898             | 22061           | 4519        | 2581        | 155            | 12990          |
| Run-3             | 10114            | 21815           | 4562        | 2590        | 148            | 12837          |
| Run-4             | 10134            | 21907           | 4600        | 2542        | 144            | 13027          |
| Run-5             | 11140            | 21381           | 5295        | 2519        | 160            | 13208          |
| Run-6             | 10564            | 22175           | 4697        | 2654        | 158            | 13232          |
| ACVG              | 10388            | 21902           | 4738        | 2593        | 153            | 13027          |
| STDV              | 442              | 285             | 286         | 48          | 6              | 166            |
| RSD (%)           | 4.26             | 1.30            | 6.05        | 1.86        | 3.98           | 1.28           |

IPA: Isopropyl alcohol, MDC: Methylene dichloride, LOQ: Limit of quantitation
### Table 7: LOQ-precision data

| No. of injections | Area of methanol | Area of acetone | Area of IPA | Area of MDC | Area of benzene | Area of toluene |
|-------------------|------------------|-----------------|-------------|-------------|----------------|-----------------|
| Run-1             | 10441            | 22071           | 4752        | 2609        | 152            | 12865           |
| Run-2             | 9898             | 22061           | 4519        | 2581        | 155            | 12990           |
| Run-3             | 10114            | 21815           | 4562        | 2590        | 148            | 12837           |
| Run-4             | 10134            | 21907           | 4600        | 2542        | 144            | 13027           |
| Run-5             | 11140            | 21381           | 5295        | 2519        | 160            | 13208           |
| Run-6             | 10564            | 22175           | 4697        | 2654        | 158            | 13232           |
| ACGV              | 10382            | 21902           | 4738        | 2583        | 153            | 13027           |
| STDV              | 442              | 285             | 286         | 48          | 6              | 166             |
| RSD (%)           | 4.26             | 1.30            | 6.05        | 1.86        | 3.98           | 1.28            |

IPA: Isopropyl alcohol, MDC: Methylene dichloride, LOQ: Limit of quantitation

### Table 8: Recovery data for six organic volatile impurities

| OVs          | Average sample area (n=3) | Average STD area (n=3) | Average 50% area (n=3) | Average 100% area (n=3) | Average 150% area (n=3) | % recovery at 50, 100, and 150% |
|--------------|---------------------------|------------------------|-------------------------|--------------------------|--------------------------|---------------------------------|
| Methanol     | 20,720                    | 423,293                | 218,883                 | 448,403                  | 677,886                  | 50 93.63 100 101.04 150 103.50 |
| Acetone      | 6248                      | 864,027                | 429,669                 | 879,057                  | 1,322,004                | 50 98.01 100 101.02 150 101.52 |
| IPA          | ND                        | 161,308                | 80,444                  | 173,348                  | 264,440                  | 50 107.46 100 107.46 150 109.29 |
| MDC          | ND                        | 96,789                 | 51,465                  | 149,711                  | 264,440                  | 50 106.34 100 103.47 150 103.12 |
| Benzene      | ND                        | 2695                   | 1451                    | 2750                     | 4161                     | 50 107.68 100 102.04 150 102.93 |
| Toluene      | ND                        | 522,898                | 263,573                 | 543,064                  | 827,234                  | 50 100.81 100 103.86 150 105.47 |

IPA: Isopropyl alcohol, MDC: Methylene dichloride, LOQ: Limit of quantitation

### Table 9: Recovery data at LOQ level

| No. of injections | Area of methanol | Area of acetone | Area of IPA | Area of MDC | Area of benzene | Area of toluene |
|-------------------|------------------|-----------------|-------------|-------------|----------------|-----------------|
| Run-1             | 31,574           | 29,689          | 5283        | 2670        | 157            | 14,391          |
| Run-2             | 31,742           | 27,624          | 5277        | 2775        | 164            | 14,530          |
| Run-3             | 31,674           | 29,144          | 5600        | 2727        | 152            | 14,879          |
| Average area      | 31,663           | 28,819          | 5387        | 2724        | 158            | 14,600          |
| STD avg. area (n=6) | 10,382       | 21,902          | 4738        | 2583        | 153            | 13,027          |
| In sample avg. area (n=3) | 20,720     | 6248            | ND          | ND          | ND             | ND              |
| % recovery        | 105.41          | 103.05          | 113.69      | 105.46      | 103.05         | 112.07          |

IPA: Isopropyl alcohol, MDC: Methylene dichloride, LOQ: Limit of quantitation

### Table 10: Ruggedness data for six organic volatile impurities

| Different days and analysts | %RSD for methanol | %RSD for acetone | %RSD for IPA | %RSD for MDC | %RSD for benzene | %RSD for toluene |
|---------------------------|------------------|-----------------|-------------|-------------|-----------------|-----------------|
| Day-1                     | Analyst-1        | 3.91            | 2.03        | 3.00        | 4.37            | 4.03            | 3.29            |
|                          | Analyst-2        | 7.69            | 4.53        | 3.30        | 5.27            | 4.4             | 2.56            |
|                          | Analyst-1 and 2  | 5.81            | 3.64        | 7.41        | 4.83            | 4.21            | 2.81            |
| Day-2                     | Analyst-1        | 7.05            | 2.09        | 3.76        | 8.27            | 5.86            | 2.34            |
|                          | Analyst-2        | 8.54            | 3.39        | 5.06        | 3.09            | 5.56            | 1.53            |
|                          | Analyst-1 and 2  | 7.48            | 2.88        | 4.52        | 6.77            | 5.03            | 1.93            |
|                          | Day-1 and 2      | 6.8             | 2.32        | 8.67        | 6.6             | 4.83            | 3.36            |
|                          | Day-1 and 2      | 8.48            | 3.91        | 4.08        | 4.92            | 4.92            | 3.21            |

IPA: Isopropyl alcohol, MDC: Methylene dichloride
**Table 11: Robustness data for six organic volatile impurities**

| Name of OVI's | Flow rate (mL/min) | Vial condition temperature (°C) |
|---------------|--------------------|---------------------------------|
|               | 2.5 mL/min (RSD %) | 3.1 mL/min (RSD %) | 75°C (RSD %) | 85°C (RSD %) |
| Methanol      | 9.47               | 5.02               | 3.84          | 4.83          |
| Acetone       | 3.60               | 1.62               | 3.19          | 6.23          |
| IPA           | 9.66               | 6.61               | 6.27          | 2.86          |
| MDC           | 5.01               | 4.72               | 2.15          | 3.48          |
| Benzene       | 5.16               | 3.05               | 3.76          | 2.57          |
| Toluene       | 2.53               | 3.04               | 3.23          | 3.50          |

IPA: Isopropyl alcohol, MDC: Methylene dichloride

**Table 12: Six organic volatile impurities content in tablet analysis**

| Name of drug | Label claim (mg) | Methanol (ppm) | Acetone (ppm) | IPA (ppm) | MDC (ppm) | Benzene (ppm) | Toluene (ppm) |
|--------------|------------------|---------------|---------------|-----------|-----------|---------------|---------------|
| Sumatriptan  | 100              | Not detected  | Not detected  | Not detected | Not detected | Not detected  | Not detected  |

IPA: Isopropyl alcohol, MDC: Methylene dichloride

**Table 13: Solution stability data for six OVI’s and sumatriptan succinate API**

| Methanol (h) | Area in standard | % solution stability for standard | Area in sample | % solution stability for API sample |
|--------------|------------------|----------------------------------|----------------|-----------------------------------|
| At 0         | 429,510          | Not applicable                    | 23,615         | Not applicable                    |
| At 12        | 418,456          | 97.43                            | 23,516         | 99.58                            |
| At 24        | 409,560          | 95.36                            | 23,356         | 99.32                            |
| Acetone (h)  | Area in standard | % solution stability for standard | Area in sample | % solution stability for API sample |
| At 0         | 852,456          | Not applicable                    | 7325           | Not applicable                    |
| At 12        | 839,521          | 98.48                            | 7295           | 99.59                            |
| At 24        | 824,562          | 96.73                            | 7245           | 99.31                            |
| IPA (h)      | Area in standard | % solution stability for standard | Area in sample | % solution stability for API sample |
| At 0         | 1658,845         | Not applicable                    | Not detected   | Not applicable                    |
| At 12        | 161,450          | 97.14                            | Not detected   | Not applicable                    |
| At 24        | 160,125          | 96.53                            | Not detected   | Not applicable                    |
| MDC (h)      | Area in standard | % solution stability for standard | Area in sample | % solution stability for API sample |
| At 0         | 942,15           | Not applicable                    | Not detected   | Not applicable                    |
| At 12        | 2515             | 95.09                            | Not detected   | Not applicable                    |
| At 24        | 2499             | 94.48                            | Not detected   | Not applicable                    |
| Benzene (h)  | Area in standard | % solution stability for standard | Area in sample | % solution stability for API sample |
| At 0         | 2645             | Not applicable                    | Not detected   | Not applicable                    |
| At 12        | 2515             | 95.09                            | Not detected   | Not applicable                    |
| At 24        | 2499             | 94.48                            | Not detected   | Not applicable                    |
| Toluene (h)  | Area in standard | % solution stability for standard | Area in sample | % solution stability for API sample |
| At 0         | 521,325          | Not applicable                    | Not detected   | Not applicable                    |
| At 12        | 509,523          | 97.74                            | Not detected   | Not applicable                    |
| At 24        | 501,236          | 96.15                            | Not detected   | Not applicable                    |

IPA: Isopropyl alcohol, MDC: Methylene dichloride, OVI's: Organic volatile impurities, API: Active pharmaceutical ingredients

**Sumatriptan succinate tablet analysis**

The prepared sumatriptan succinate tablet solution (250 mg/mL) was injected. The six organic volatile impurities content in sumatriptan succinate tablets was found within the specifications. The results and typical chromatograms were shown in Table 12 and Fig. 9.

**Solution stability**

Stability of six organic volatile impurities standard and sumatriptan succinate API sample prepared in DMSO as a diluent. Three-time intervals solutions (initial, after 12 h, and after 24 h) were prepared on the same day and keep them at room temperature. Initial, after 12 h, and after 24 h OVI’s standard and sumatriptan succinate API solutions were injected at that time point. Then, the calculated the % of solution stability for the area of initial, after 12 h, and after 24 h OVI’s standard and sumatriptan succinate API solutions were within the specifications. The results and typical chromatograms were shown in Table 12 and Fig. 9.

**CONCLUSION**

The six OVI’s, methanol, acetone, IPA, dichloromethane, benzene, and toluene, were well separated from each other and quantified by the proposed method. This method was also applied for the quantification of organic volatile impurities in the marketed sumatriptan succinate, which were present in ppm specification limits as per ICH guidelines. The proposed method was validated as per the ICH guidelines and the results revealed that the method was scientifically. This investigation may be helpful to the manufacturers for controlling and minimization of the organic volatile impurities. Moreover, this method was found to be applicable for the routine analysis of the sumatriptan succinate in the pharmaceutical industry.

**AUTHORS’ CONTRIBUTIONS**

Dr. K. Prasada Rao supervised the manuscript preparation and reviewed the manuscript. I would like to thank the whole staff of the Chemistry Department of Bapatla Engineering College for their technical support and productive discussions.
AUTHORS’ FUNDING

I would like to thank to Chemistry department of Bapatla Engineering College for their Financial support.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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