# METHOD DEVELOPMENT, VALIDATION AND STABILITY STUDY FOR SIMULTANEOUS ESTIMATION OF TELMISARTAN AND INDAPAMIDE BY REVERSE PHASE-HIGH PERFORMANCE LIQUID CHROMATOGRAPHY IN PURE AND MARKETED FORMULATION.

Patel Amit R[1*], Chandrul Kaushal Kishor [2]

1 Department of Pharmaceutical Analysis Jaipur National University, Jagatpura, Jaipur 302025, Rajashthan, India.

2 Department of Pharmaceutical Analysis Jaipur National University, Jagatpura, Jaipur 302025, Rajashthan, India.

**ABSTRACT**

An approach of forced degradation study was successfully applied for the development of a stability-indicating assay method for simultaneous determination of telmisartan and indapamide in a formulation in the presence of its degradation products. The method showed adequate separation of Telmisartan and indapamide from their associated main impurities and degradation products. Separation was achieved on an Amazone C18, 5 microm, 150 x 4.6 mm the mobile phase (Buffer: acetonitrile: methanol) (45+25+30) KH2PO4 & Triethaylamine Ph 3.0 with ortho phosphoric acid buffer flow rate of 1 mL/min and UV detection at 285 nm. Comprehensive stress testing of telmisartan and indapamide Rt= 4.7 min, 10.7 min was according to the International Conference on Harmonization (ICH) guideline Q1A (R2). The drug was subjected to acid hydrolysis, base hydrolysis, to apply stress conditions. There were no other coeluting, interfering peaks from excipients, impurities. The method was validated in terms of linearity, precision, accuracy, specificity, robustness, and solution stability. The linearity of the proposed method was investigated in the range of 6-22.5 microg/mL (r2 = 0.999) for telmisartan and 11.2-42 microg/mL (r2 = 0.9997) for indapamide.

**KEYWORDS**: Telmisartan, Indapamide, Stress degradation, RP-HPLC, Validation

**INTRODUCTION:**

Telmisartan [1] angiotensin converting enzyme (ACE), Telmisartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II [2] by selectively blocking the binding of angiotensin II to the AT1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Telmisartan is indicated for the treatment of hypertension. Chemically known as 4'-[(1,4'-di methyl-2'-propyl [2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid The molecular structure of Telmisartan is shown in Figure 1

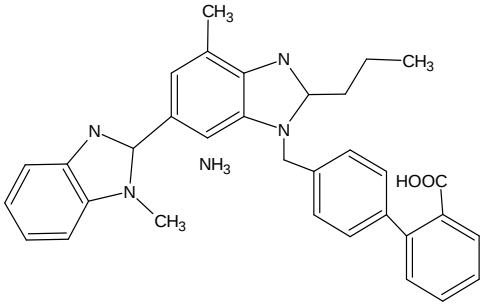



Figure 1

Indapamide [3] a benzamide- Sulfonamide-indole. It is called a thiazide-like diuretic and it is an antihypertensive and a diuretic. Chemically known as 4-chloro-N-(2-methyl-2,3-dihydroindol-1-yl)-3-sulfamoyl-benzamide The molecular structure of Indapamide is shown in Figure 2

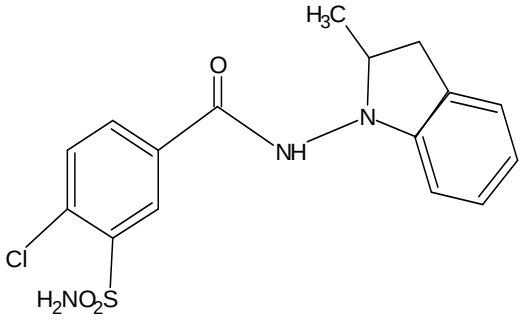



Figure 2

Simultaneous Telmisartan and Indapamide is not official in any Pharmacopoeia. Literature study reveals that a UV and HPLC method and individual are available for estimation of Telmisartan and Indapamide. Moreover there is no stability indicating assay method developed for the estimation of Telmisartan and Indapamide and its formulations.

The drug stability test guidelines Q1A (R2) [4] issued by International Conference on Harmonization (ICH) requires that analytical test procedures for stability samples should be fully validated and the assays should be stability indicating. The aim of the present study accordingly was to establish inherent stability of the following two drugs in combination viz. Telmisartan and Indapamide through stress studies under a variety of ICH recommended test conditions and to develop and validate stability indicating assay method. There is no report yet of stability indicating RP-HPLC method for these drugs in combination.

The objective of this work was to develop inexpensive, simple and rapid stability indicating RP-HPLC methods which would be accurate and precise.

The methods were validated according to ICH guidelines. The linearity of response, accuracy, and intermediate precision of the described methods have been validated.

**MATERIALS AND METHODS:**

1) Telmisartan (TELMI): - Working standard grade was gifted by MAITHRI LABORATORY PVT LTD. (Andhr a Pradesh, India) and it's claimed purity was 99.0%.
2) Indapamide (INDA): - Working standard grade was supplied by AMI LIFE SCIENCES PVT LTD. (Baroda, India) and it's claimed purity was 98.5%.
3) Telmisartan and Indapamide Active Pharmaceutical Ingredient (API) were supplied by Cadilla Healthcare Limited (Ahmedabad, India).
4) Marketed formulation Inditel-d (telmisartan + indapamide) 40mg and 1.5mg claim Cadila Healthcare Limited (Ahmedabad, India).

**Reagents**

1) Methanol:-HPLC grade, Fisher scientific pvt. Ltd.
2) Acetonitrile: - HPLC grade, Spectrochem pvt. Ltd., Mumbai.
3) Milli-Q water: - It was purified by Millipore Corporation's system mfg Barnsead.
4) Triethylamine: - AR grade, Spectrochem Pvt Ltd, India.
5) Orthophosphoric acid:-AR grade, Fisher scientific pvt. Ltd.
6) Potassium Dihydrogen Phosphate:- AR grade, Merck Specialities Pvt. Ltd.
7) 1 N Hydrochloric acid: - Merck, India.
8) 0.1 N Sodium hydroxide: - Merck, India.
9) Hydrogen Peroxide (30%):- Merck, India.

**HPLC System**

A Shimadzu HPLC system equipped with LC-10AVP UV- visible detector

**Chromatographic Condition:**

Column: Amzone C18, 150 mm × 4.6 mm i.d.

Mobile Phase: Buffer: Acetonitrile: Methanol (45:25:30)

Flow: 1 ml/ min

Injection Volume: 20 µl

Detection: 285 nm

Oven temperature: 30°C

Run time: 15 min

Diluent used: Mobile Phase

**Experimental Work and Condition [5-7]**

**Buffer Solution:** 6 g of Potassium dihydrogen phosphate was accurately weighed an dissolved in 1000 mL of Milli Q water add 2ml Triethaylamine then adjust ph 3 with OPA Ortho phosphoric acid.

**Mobile Phase**: Buffer: Acetonitrile: Methanol

(45:25:30 V/V)

**Preparation of Standard Solution:** The standard stock of Telmisartan (30ppm) and Indapamide (16ppm) was prepared by dissolving 60 mg and 32 mg of working standard in Methanol in 200 mL volumetric flask After sonicate for 2 min and volume was made up to the mark with methanol. 5 mL aliquot from the standard stock solution of Telmisartan and Indapamide was transferred in 50 mL volumetric flask, and the volume was made up to the mark with diluent.

**Sample Preparation:** Twenty capsule were weighed, their mean weight was determined, and they were crushed in a mortar. An amount of powdered mass Telmisartan equivalent to 80 mg and Indapamide equivalent to 7.5 mg weighed. First seprate the Telmisartan Tablet from capsule cruse and take equivalent to 80 mg add methanol 70 ml sonicate 30 min in another seprate the Indapamide Tablets from Capsule equivqlent to 7.5 mg then add 10 ml solution of telmisartan stock solution then add 40 ml methanol sonicate 30 min and make upto mark with diluent in 250ml volumetric flask.

**Stress Degradation studies:**

Acid degradation: Treated with 5ml 5 N HCl and heated on boiling water bath for 2 hours then cool at room temperature afte that add 5ml 5 N NAOH for neutralize the solution.

Alkali degradation: Treated with 5ml 5 N NaOH and heated on boiling water bath for 2 hours then cool at room temperature afte that add 5ml 5 N HCl for neutralize the solution.

**RESULTS AND DISCUSSION**:

Literature review reveals only individual methods for estimation of Indapamideand Telmisartan but no methods were reported for simultaneous estimation and Stability study of Indapamide and Telmisartan. A simple, precise, accurate, RP-HPLC method has been developed for the estimation of Indapamide and Telmisartan in bulk and in Capsule formulation. The UV detection was carried out as 285nm as Telmi and Inda showed very good absorbance at this wavelength. An chromatogram of Telmi and Inda shown in fig-1, Indapamide and Telmisartan with retention time of 4.7 min and 10.7 min respectively.

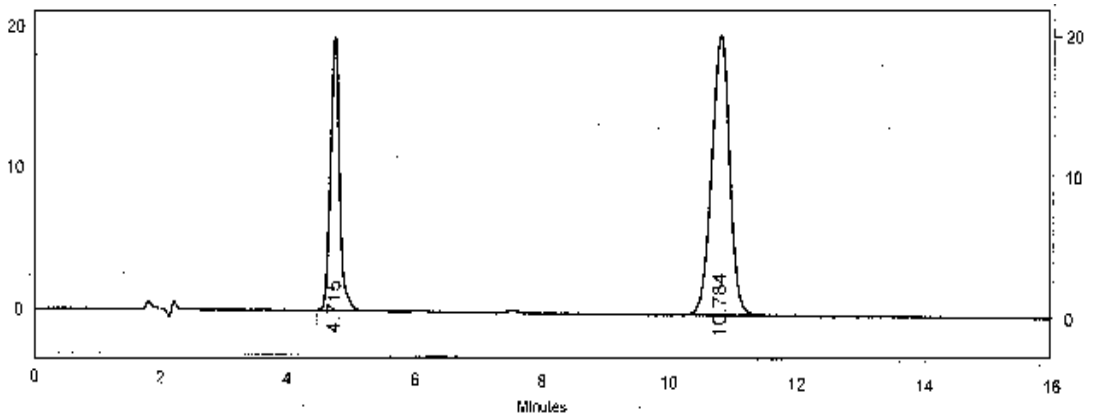



Figure 1

**Stress Degradation studies:**

**Acid degradation**:

**Standard preparation for acid degredation**

Take 60mg Telmisartan and seprate taken Indapamide 32mg then add 5N HCL in 200 mL volumetric flask heated on boiling water bath for 2 hours then cool at room temperature afte that add 5ml 5 N NAOH for neutralize the solution and volume was made up to the mark with methanol. 5 mL aliquot from the standard stock solution of Telmisartan and Indapamide was transferred in 50 mL volumetric flask, and the volume was made up to the mark with diluent.

**Sample preparation for acid degredation**

Twenty capsule were weighed, their mean weight was determined, and they were crushed in a mortar. An amount of powdered mass Telmisartan equivalent to 80 mg and Indapamide equivalent to 7.5 mg weighed. First seprate the Telmisartan Tablet from capsule cruse and take equivalent to 80 mg add 5N HCL in 200 mL volumetric flask heated on boiling water bath for 2 hours then cool at room temperature afte that add 5ml 5 N NAOH for neutralize the solution add methanol 70 ml sonicate 30 min in another seprate the Indapamide Tablets from Capsule equivqlent to 7.5 mg then add 5N HCL in 250 mL volumetric flask heated on boiling water bath for 2 hours then cool at room temperature afte that add 5ml 5 N NAOH for neutralize the solution add 10 ml solution of telmisartan stock solution then add 40 ml methanol sonicate 30 min and make upto mark with diluent in 250ml volumetric flask same preparation of placebo only drug is not add in preparation.

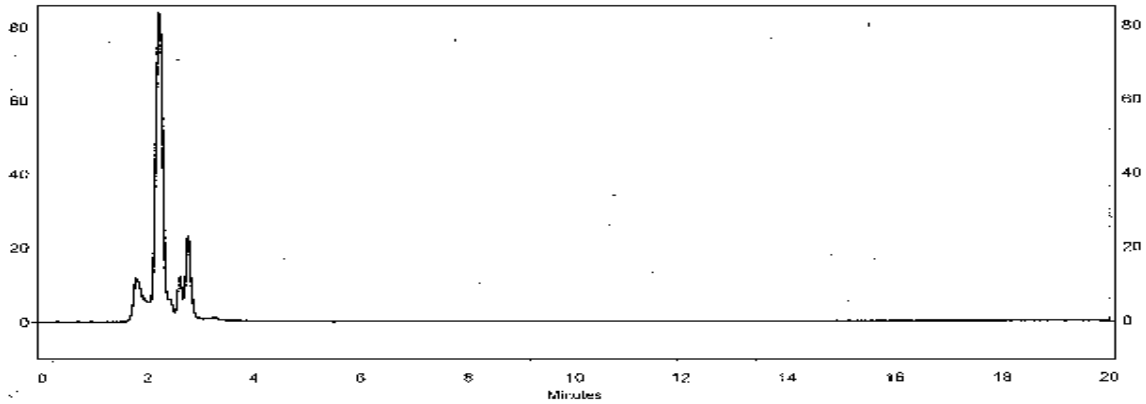



Figure 2 Chromatograms of acid hydrolysis-degraded placebo

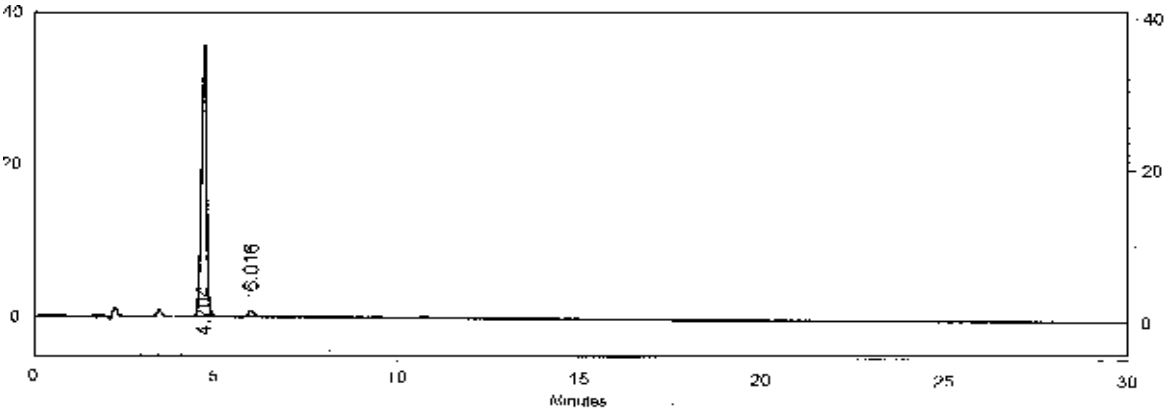



Figure 3 Chromatograms of acid hydrolysis-degraded, INDA standard

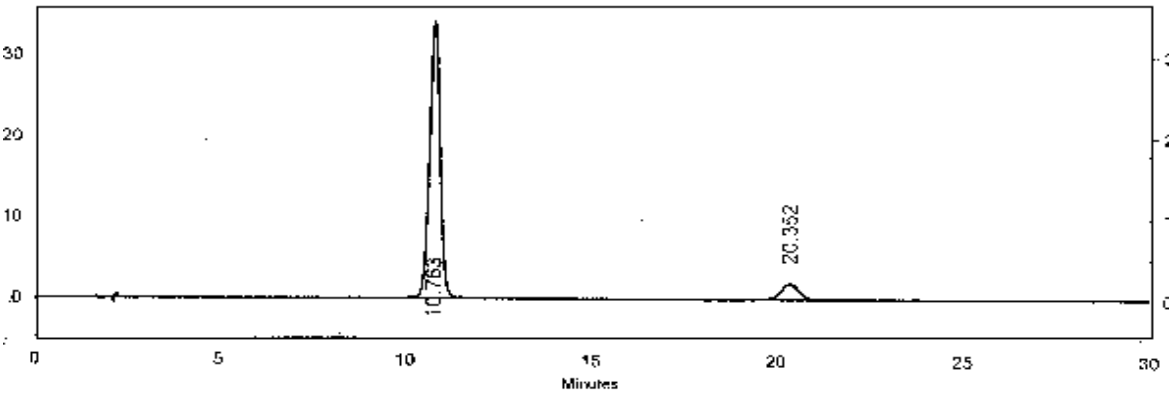



Figure 4 Chromatograms of acid hydrolysis-degrad, TELMI standard

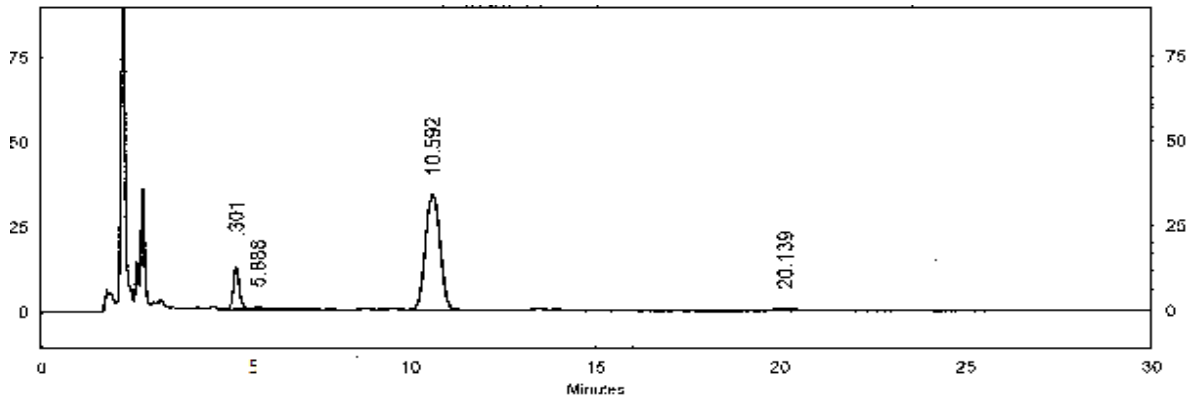



Figure 5 Chromatograms of acid hydrolysis-degraded sample preparation

**Alkali (base) degradation:**

**Standard preparation for alkali degredation**

Take 60mg Telmisartan and seprate taken Indapamide 32mg then add 5N NAOH in 200 mL volumetric flask heated on boiling water bath for 2 hours then cool at room temperature afte that add 5ml 5 N HCL for neutralize the solution and volume was made up to the mark with methanol. 5 mL aliquot from the standard stock solution of Telmisartan and Indapamide was transferred in 50 mL volumetric flask, and the volume was made up to the mark with diluents.

**Sample preparation for alkali degredation**

Twenty capsule were weighed, their mean weight was determined, and they were crushed in a mortar. An amount of powdered mass Telmisartan equivalent to 80 mg and Indapamide equivalent to 7.5 mg weighed. First seprate the Telmisartan Tablet from capsule cruse and take equivalent to 80 mg add 5N NAOH in 200 mL volumetric flask heated on boiling water bath for 2 hours then cool at room temperature afte that add 5ml 5 N HCL for neutralize the solution add methanol 70 ml sonicate 30 min in another seprate the Indapamide Tablets from Capsule equivqlent to 7.5 mg then add 5N NAOH in 250 mL volumetric flask heated on boiling water bath for 2 hours then cool at room temperature afte that add 5ml 5 N HCL for neutralize the solution add 10 ml solution of telmisartan stock solution then add 40 ml methanol sonicate 30 min and make upto mark with diluent in 250ml volumetric flask same preparation of placebo only drug is not add in preparation.

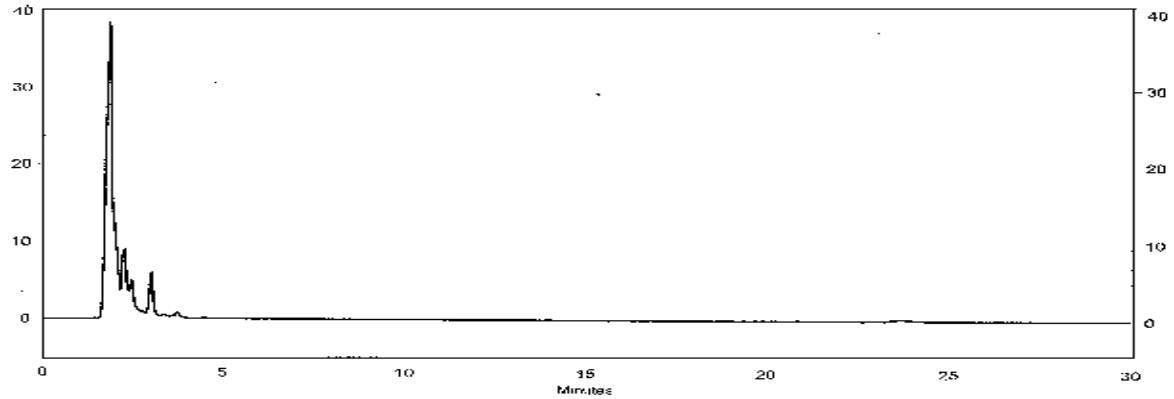



Figure 6: Chromatograms of Alkali (base) hydrolysis-degraded placebo

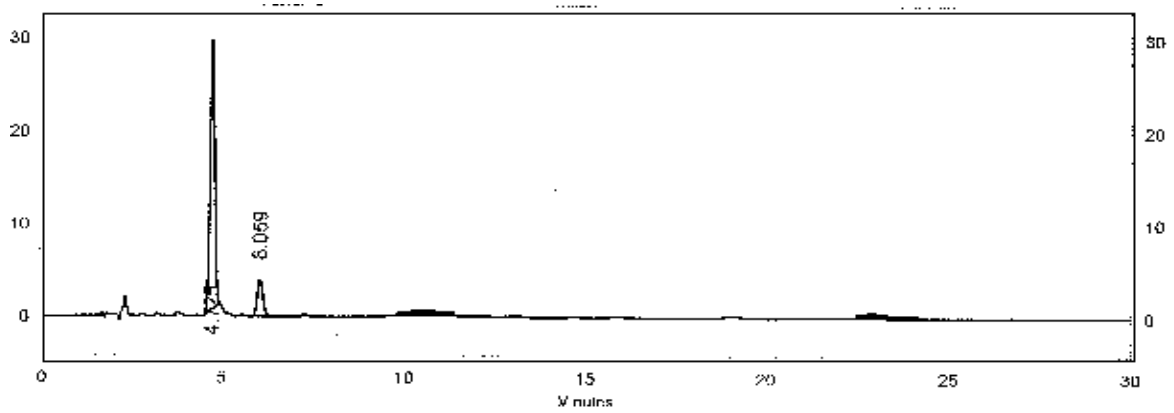



Figure 7: Chromatograms of Alkali (base) hydrolysis-degraded INDA standard

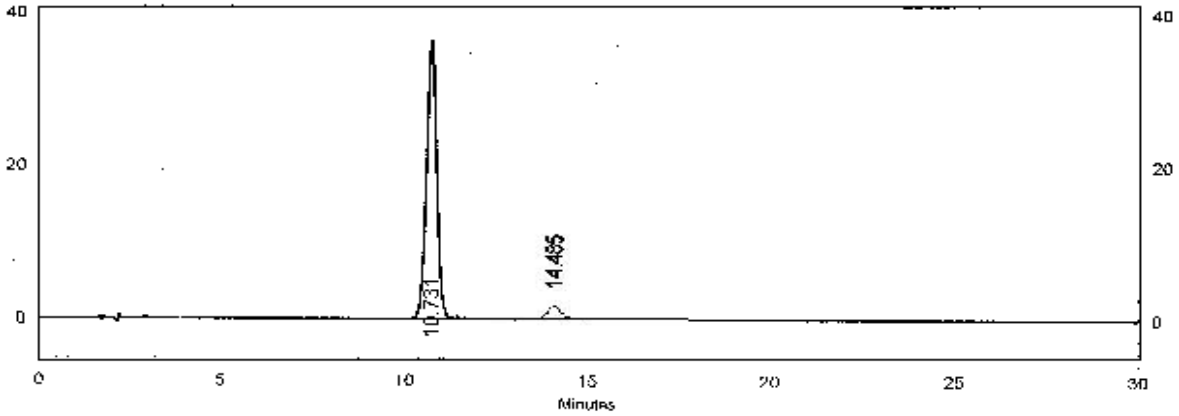



Figure 8: Chromatograms of Alkali (base) hydrolysis-degraded TELMI standard

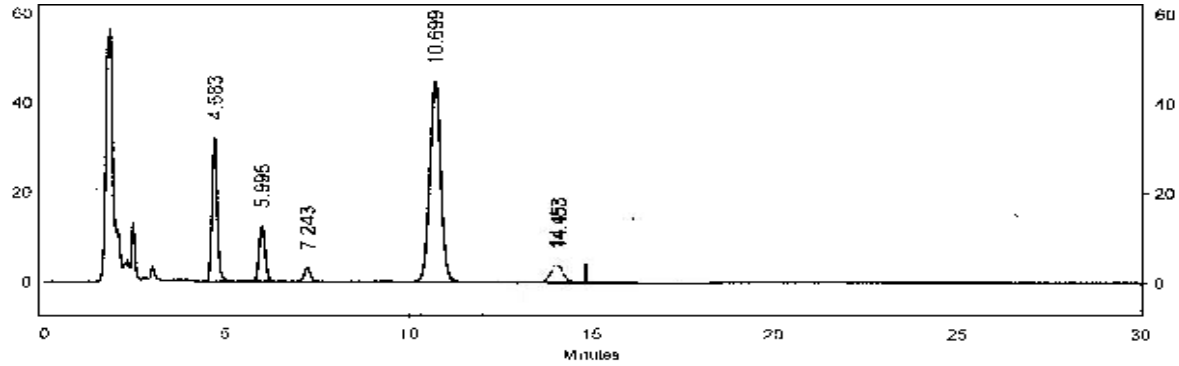



Figure 9: Chromatograms of Alkali (base) hydrolysis-degraded sample preparation.

| Stress condition/ duration/ state | % Area | | % Degradation | | Peak Purity Index | |
|---|---|---|---|---|---|---|
| | INDA | TELM | INDA | TELM | INDA | TELM |
| Acidic/5N HCl/100°C/2hr/ solution/ 5N NAOH | 96.3 | 90.62 | 4.2 | 9.86 | 1 | 1 |
| Alkaline/ 5 N NaOH /100 °C /2hr/solution/ 5N HCL | 86.32 | 97.87 | 13.68 | 3.13 | 1 | 1 |

Table 1 Results of forced degradation study of standard the proposed method, indicating specificity of the developed method

| Stress condition/ duration/ state | % Area | | % Degradation | | Peak Purity Index | |
|---|---|---|---|---|---|---|
| | INDA | TELM | INDA | TELM | INDA | TELM |
| Acidic/5 N HCl/100°C/2hr/ solution | 98.2 | 99.0 | 2.1 | 1.3 | 1 | 1 |
| Alkaline/ 5 N NaOH / 100°C /3 hr/solution | 83.9 | 89.7 | 15.8 | 12.4 | 1 | 1 |

Table 2: Results of forced degradation study of sample the proposed method, indicating specificity of the developed method

**METHOD VALIDATION:**

Validation was carried out with respect to various parameters, as required under ICH guidelineQ2 (R1).[21] The developed method validated with respect to parameters such as linearity,precision, accuracy, specificity, ruggedness, robustness and solution stability[8].

**System suitability and system precision**

System suitability and system precision was daily performed during entire validation of this method. The results of system suitability and system precision were presented.

| Sr. No. | Parameters | INDAPAMIDE | TELMISARTAN |
|---|---|---|---|
| 1 | Peak area | 429165 | 742618 |
| 2 | No. of theoretical plates | 5681 | 7304 |
| 3 | Retention time (min) | 4.7 | 10.7 |
| 4 | Asymmetry | 1.32 | 1.07 |
| 5 | % RSD | 0.5 | 0.9 |

Table 3 Mean values of system suitability parameters

**Linearity**

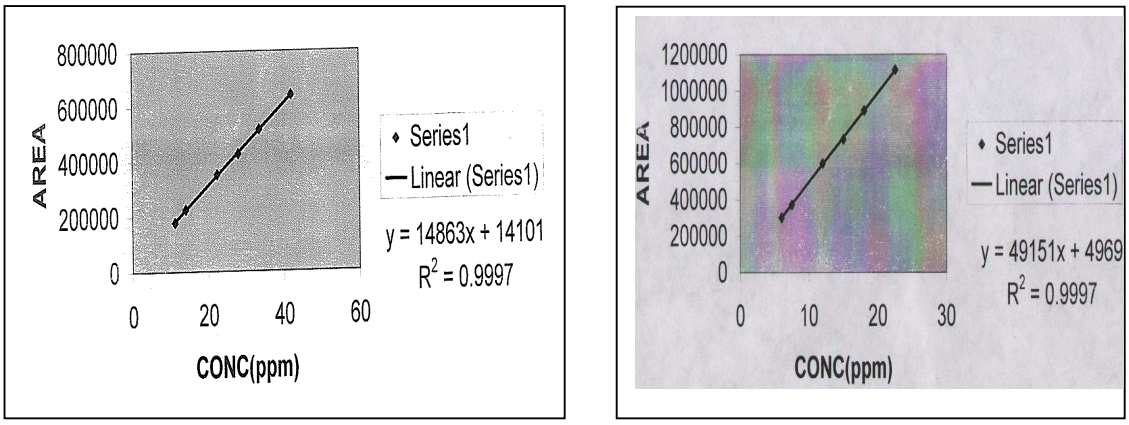
The linearity was determined at six levels over the range of 40% to 150% of standard concentration. TEMI and INDA standard stock solutions were prepared. INDA standard stock solutions, aliquots of 11.2, 14, 22.4, 28, 33.6 and 42ml and TELMI standard stock solutions, aliquots of 2, 2.5, 4, 5, 6 and 7.5ml

| Linearity level | Conc. ( µg/ml ) | Repetitions Area | Mean Area |
|---|---|---|---|
| Level – 1 (40%) | 11.2 | 300016 | 177051 |
| | | 300091 | |
| Level – 2 (50%) | 14 | 222495 | 224743 |
| | | 226990 | |
| Level – 3 (80%) | 22.4 | 347147 | 350654 |
| | | 354161 | |
| Level – 4 (100%) | 28 | 421712 | 425972 |
| | | 430232 | |
| Level – 5 (120%) | 33.6 | 508577 | 513714 |
| | | 518851 | |
| Level – 6 (150%) | 42 | 632789 | 639181 |
| | | 645573 | |
| % RSD | | | 1.2 |
| Correlation coefficient | | | 0.9997 |

Table 4 Linearity of INDAPAMIDE by RP-HPLC method

| Linearity level | Conc. ( µg/ml ) | Repetitions Area | Mean Area |
|---|---|---|---|
| Level – 1 (40%) | 6 | 300016 | 300054 |
| | | 300091 | |
| Level – 2 (50%) | 7.5 | 367152 | 370861 |
| | | 374570 | |
| Level – 3 (80%) | 12 | 593192 | 599184 |
| | | 605176 | |
| Level – 4 (100%) | 15 | 724869 | 732191 |
| | | 739513 | |
| Level – 5 (120%) | 18 | 887695 | 891260 |
| | | 894825 | |
| Level – 6 (150%) | 22.5 | 1112583 | 1114813 |
| | | 1117043 | |
| % RSD | | | 1.6 |
| Correlation coefficient | | | 0.9997 |

Table 5 Linearity of TELMISARTAN by RP-HPLC method




Indapamide Telmisartan

Figure 10 Linearity and calibration curve

**Precision**[9]

The method precision was done by preparing six different sample preparations by one analyst under the same condition. The results were presented in Table 5. The results obtained were within 2% RSD.

**Ruggedness**

Ruggedness test was determined between two different analysts, instruments and Columns. The value of percentage RSD was below 2.0%, showed ruggedness [10] of developed analytical method. The results were presented in Table 5.

| Parameters | Indapamide | | Telmisartan | |
|---|---|---|---|---|
| | %Assay | % RSD | %Assay | % RSD |
| Method | 101.4 | 1.1 | 98.4 | 0.7 |
| Ruggedness | 100.5 | 1.5 | 99.0 | 0.9 |

Table 6: Results of Method Precision and Ruggedness

**Accuracy**

The difference between theoretical added amount and practically achieved amount is called accuracy of analytical method. Accuracy [11] was determined at three different level 50%, 100% and 150% of the target concentration in triplicate. Results of Accuracy Data of Indapamide

| Level of Recovery | Area | Added Amount (mg) | Recovered Amount (mg) | % Recovery | Mean % Recovery | % RSD |
|---|---|---|---|---|---|---|
| 50% | 223530 | 233.4 | 230.4 | 100.3 | 100.7 | 0.4 |
| | 223127 | 216 | 229.8 | 100.8 | | |
| | 237179 | 246 | 244.8 | 101.0 | | |
| 100% | 392078 | 422.4 | 404.4 | 97.3 | 98.9 | 1.4 |
| | 428148 | 450 | 441.6 | 99.6 | | |
| | 425300 | 445.8 | 438.6 | 99.9 | | |
| 150% | 601149 | 651 | 619.8 | 96.6 | 98.2 | 1.5 |
| | 584571 | 621 | 602.4 | 98.5 | | |
| | 573488 | 602.4 | 591 | 99.6 | | |

Table 7: Results of accuracy Data of Indapamide

| Level of Recovery | Area | Added Amount (mg) | Recovered Amount (mg) | % Recovery | Mean % Recovery | % RSD |
|---|---|---|---|---|---|---|
| 50% | 371804 | 116.5 | 114.4 | 99.2 | 99.4 | 0.2 |
| | 352255 | 110 | 108.4 | 99.5 | | |
| | 351229 | 109.8 | 108.7 | 99.4 | | |
| 100% | 692691 | 214.9 | 213.1 | 100.2 | 100.1 | 0.1 |
| | 699893 | 217.3 | 215.4 | 100.1 | | |
| | 695983 | 216.3 | 214.2 | 100 | | |
| 150% | 1014052 | 316.85 | 312.1 | 98.5 | 98.1 | 0.4 |
| | 1006200 | 315.70 | 309.6 | 98.1 | | |
| | 1001526 | 315.16 | 308.26 | 97.8 | | |

Table 8: Results of Accuracy Data of Telmisartan

**Solution stability**[12-13]**:**

The standard and sample solutions were found stable up to 24 hours at room temperature. After 2, 6, 12, 16, 20, 24 hours the solutions were analysed. No significant changes (<2%) were observed for the chromatographic responses for the solution analysed, relative to freshly prepared standard. Results related to solution stability are summarized in Table 9,10.

| Time (hrs) | INDAPAMIDE | | TELMISARTAN | |
|---|---|---|---|---|
| | Area | % Difference | Area | % Difference |
| Initial | 374035 | - | 734389 | - |
| 2 | 375233 | 0.3 | 732872 | -0.1 |
| 6 | 375601 | 0.4 | 737011 | 0.3 |
| 12 | 378456 | 1.1 | 735685 | 0.1 |
| 16 | 371106 | -0.7 | 733658 | -0.2 |
| 20 | 374565 | 0.1 | 735065 | -0.1 |
| 24 | 370564 | -0.6 | 732214 | -0.7 |

Table 9*:* Solution stability data for standard preparation

| Time (hrs) | INDAPAMIDE | | TELMISARTAN | |
|---|---|---|---|---|
| | Area | % Difference | Area | % Difference |
| Initial | 383859 | - | 722384 | - |
| 2 | 382974 | -0.2 | 718751 | -0.5 |
| 6 | 380850 | -0.8 | 720307 | -0.3 |
| 12 | 383340 | -0.1 | 723934 | 0.2 |
| 16 | 383102 | -0.2 | 724071 | 0.2 |
| 20 | 381297 | -0.7 | 721790 | -0.1 |
| 24 | 382385 | -0.4 | 720214 | -0.3 |

Table 10*:* Solution stability data for sample preparation

**Robustness**

Robustness[14-15] of the method was carried out by deliberately made small change in the flow rate, pH, organic phase ratio and column oven temperature[16-17]. Results were presented in Table 11,12.

| Sr. No | Sys. Suit. | Temp. -5°C | Temp. +5°C | Flow -10% | Flow +10% | Org. - 2% | Org. +2% | pH = 3.3 | pH = 2.7 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 374035 | 377338 | 375454 | 419921 | 342333 | 384115 | 325743 | 375574 | 356893 |
| 2 | 375233 | 378583 | 375450 | 419271 | 354874 | 375528 | 336985 | 369854 | 353689 |
| 3 | 375601 | 387954 | 380902 | 420158 | 345896 | 380546 | 329857 | 375485 | 354874 |
| 4 | 371110 | 378995 | 378965 | 419852 | 351247 | 383996 | 332154 | 370445 | 349852 |
| 5 | 377853 | 381245 | 379958 | 421005 | 341245 | 379568 | 326892 | 372548 | 350002 |
| **%RSD** | 0.9 | 1.0 | 0.6 | 1.5 | 0.9 | 0.9 | 1.2 | 0.7 | 0.8 |

Table 11: Results of Robustness study of Indapamide

| Sr. No | Sys. Suit. | Temp. -5°C | Temp. +5°C | Flow -10% | Flow +10% | Org. -2% | Org. +2% | pH = 3.3 | pH = 2.7 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 734389 | 690716 | 687145 | 768237 | 627479 | 685358 | 601808 | 695126 | 675314 |
| 2 | 738272 | 692417 | 688890 | 767477 | 627271 | 686710 | 612587 | 703526 | 665298 |
| 3 | 737011 | 691528 | 699130 | 765812 | 635847 | 684574 | 609874 | 695512 | 674129 |
| 4 | 735685 | 689254 | 691258 | 769854 | 615875 | 685958 | 602458 | 685233 | 678955 |
| 5 | 739451 | 695842 | 689852 | 766658 | 616585 | 678954 | 605985 | 697413 | 668465 |
| **%RSD** | 0.8 | 0.3 | 0.7 | 0.2 | 1.2 | 0.5 | 0.8 | 0.9 | 1.0 |

Table 12: Results of Robustness study of Telmisartan

Table 12:Summary of Validation Parameters of RP HPLC Method for Simultaneous estimation of Indapamide and Telmisartan.

| Parameter | Acceptance Crieteria | Indapamide | Telmisartan |
|---|---|---|---|
| Stability study | Degradation product was not interfering with the peak of drugs from peak purity profile study. | Complies | Complies |
| Range of Linearity Correlation Coefficient | Correlation coefficient r2 > 0.999 or 0.995 | 11.2- 42 mg/ml | 6- 22.5 mg/ml |
| LOD | S/N > 2 or 3 | 0.056 mg/ml | 0.030 mg/ml |
| LOQ | S/N > 10 | 0.28 mg/ml | 0.15 mg/ml |
| Precision | RSD < 2% | 1.2 | 1.6 |
| Intermediate Precision | RSD < 2% | 1.1 | 1.4 |
| Accuracy | Recovery 98- 102% (individual) | % recovery= 98.1 | % recovery= 100.1 |
| Specificity | 1) No intereference from blank, placebo and other degradation products with the main peak. 2) The peak purity index > 0.999 | No intereference. **Peak purity** 1)Test sample = 0.9992 2)Spiked sample = 0.9998 | No intereference. **Peak purity** 1)Test sample = 0.9998 2) Spiked sample = 0.9998 |
| Solution Stability | > 12 hour | Stable up to 24 hour %RSD = 0.3 | Stable up to 24 hour %RSD = 0.5 |
| Robustness | RSD NMT 2% in modified condition | Complies | Complies |

**CONCLUSION:**

From the above study we can conclude that the Indapamide and Telmisartan undergo degradation to different extent under different, above mentioned, stress conditions. In this study, the products formed after forced decomposition studies were resolved from the bulk drug response. From the peak purity profile studies, it was confirmed that the peak of the degradation product was not interfering with the peak of drugs. It confirms that peak for degradation product of drug can be resolved from the drug peak by this method. The developed method is simple, accurate, precise, and specific, economic. It is proposed simultaneous routine analysis of these drugs in presence of degradation products in stability study.

**ACKNOWLEDGMENT:**

The authors wish to express their gratitude to the management of Jaipur National University for providing the research facilities, M/s Maithri Laboratory Pvt Ltd, Andhra pardesh & M/s. Ami Life Sciences Pvt Ltd, Baroda for providing the Indapamide and Telmisartanl drug samples.

**REFERENCES:**

[1] Willard HH, Merritt LL, Dean JJA, Frank AS. Instrumental method of analysis. 7th Edition, CBS Publishers and Distributors, New Delhi, 1986; 321-23.
[2] Higuchi T, Brochman-Hausen E. Pharmaceutical Analysis. 6th Edition, Interscience, London, 1961;433-40.
[3] Mendham J, Denny RC, Barnes JD, Thomas M, " Vogels Text Book of Quantitative Chemical Analyisis", 6th edition, Pearson education, 2002; pp.2-10.
[4] ICH, Q1A (R2): Stability Testing of New Drug Substances and Products, International Conference on Harmonization, Geneva. 2003.
[5] Siggia S, Hanna JG. Quantitative organic Analysis via Functional Groups. 4th Edition, Interscience, Nottingholm, 1979; 231-35.
[6] Michael E, Schartz IS, Krull. Analytical method development and Validation. 2004; 25-46.
[7] Berry RI, Nash AR. Pharmaceutical Process Validation; Analytical method validation.Marcel Dekker Inc, New work, 1993, 57, 411-28.
[8] Sawicki E, Hauser TR., Stanley TW, Elbert W. *Anal Chem*. 1961, 33, 93-94
[9] AS Jadhav; DB Pathare; MS Shingare. Journal of Pharmaceutical and Biomedical Analysis,2007, 43(4), 1568-1572.
[10] P Musmade; G Subramanian; KK Srinivasan. Analytica Chimica Acta, 2007, 585(1), 103-109.
[11] SL Prabu; T Singh; A Joseph; C Dinesh Kumar; A Shirwaikar. Indian Journal of Pharmaceutical Sciences, 2007, 69(6), 819-821.
[12] BS Sastry; D Srinivasulu; H Ramana. Journal of Pharmaceutical Research and Health Care, 2009, 1(1), 25-33.
[13] RT Sane; S Menon; AY Deshpande; A Jain. Chromatographia, 2005, 61(3-4), 137-141.
[14] M Yadav; V Upadhyay; P Singhal; S Goswami; PS Shrivastav. Journal of Chromatography B, 2009, 877(8-9), 680-688.
[15] W Kang; EY Kim. Journal of Pharmaceutical and Biomedical Analysis, 2008, 46(3), 587-591.
[16] M Yadav; V Upadhyay; P Singhal; S Goswami; PS Shrivastav. Journal of Chromatography B, 2009, 877(8-9), 680-688.
[17] W Kang; EY Kim. Journal of Pharmaceutical and Biomedical Analysis, 2008, 46(3), 587-591.