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STUDY OF MPS UNDER STRESSED CONDITIONS

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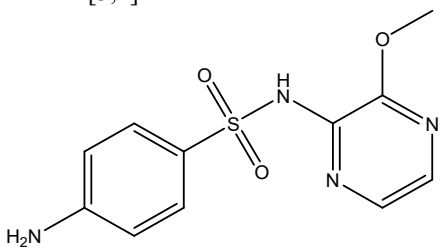
Abstract: *This study is done to access the chemical stability of the candidate compound in the pharmaceuticals. Usually, it is performed at the preliminary stage in the process of drug development. Forced degradation/ stress testing is performed under accelerated environment. The experimental conditions cause the candidate compound to degrade under extreme conditions like acid and base hydrolysis, peroxide oxidation, photo-oxidation and thermal stability to identify the resultant degradation products. This helps to establish degradation pathways and thus intrinsic stability of a drug substance. The stability of product describes shelf life and storage conditions and helps in the selection of appropriate formulations and their suitable packaging. This is compulsory for regulatory documentation. The commonly used analytical approach for FDS is HPLC with UV and/ or MS but these techniques consume a lot of time and not provide high resolution to confirm the precise detection of degradation products. Use of UPLC with photodiode array and MS analysis supports the identification of degradation products and also reduces the time needed to evolve stability indicating methods.*
Keywords *– Pharmaceuticals , Degradation, Stability Hydrolysis, Oxidation.*

1. INTRODUCTION

N1 - (3 - Methoxypyrazin - 2 - yl) sulphanilamide is a long acting sulfonamide that has been used in the treatment of urinary tract infections and respiratory due to sensitive organisms by oral route of administration.MPS is given with pyrimethamine in the treatment of malaria.[1,2]It has also been given in the ratio 4 parts of N1 - (3 - Methoxypyrazin - 2 - yl) sulphanilamide to 5 parts of trimethoprim as a combination with uses similar to those of co - trimoxazole 1.[3,4]



N^1-(3-Methoxypyrazin-2-yl)sulphanilamide

Molecular formula:$C_{11}H_{12}N_4O_3S$

Molecular Weight.: 280.3

Fig: 1 Chemical structures of solifenacin. [5]

Literature search reports few bio analytical methods for the quantitation of N1 - (3 - Methoxypyrazine - 2-yl) sulphanilamide (MPS) concentration in biological fluid samples using liquid chromatography and mass spectroscopic method.[6,7] So far, the active pharmaceutical ingredient (API) to MPS as a published report describing the complete characterization of impurities, are there.[8,9] MPS active pharmaceutical ingredient (API) in the respective objects isolation / synthesis of LC / MS / MS are no reports on the use.

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Profiling of drug substance for its impurities is a critical parameter which determines the safety of the drug substance as well as the controls required during manufacturing to ensure appropriate level of impurities.[10,11] Identification and characterization of Impurities in pharmaceutical production, the acceptable limit of 0.1 % of the present [10,12] is mandated. The present study details the identification and determination of structure of few process related impurities found in the product (MPS). [13,14]Though, different methods of synthesis of MPS are reported,[15,16] the selected route was safe, feasible & economical. However, these did not give information regarding possible impurities. Impurity profiling of drugs in pharmaceutical analysis is an important topic - the high purity of the drug substance manufacturing process technology to develop and deliver safe drugs.[17,18,19]

2. EXPERIMENTAL

Preparation of solutions for under stressed conditions was used as given below:

a)Parent sample: Take accurate quantity of about 25.00 mg of MPS in a volumetric flask of 50 cm^3 capacity add 5.0 cm^3 of diluent and sonicate to dissolve the sample and with the diluent make up the volume.(Concentration : 500 ppm)

b)Acid Hydrolysis: Take accurate quantity of about 25.00 mg of MPS in a volumetric flask of 50 cm^3 capacity. Add 5.0 cm^3 of 1N Hydrochloric acid, heat at 60 degree Celsius in water bath for 3 hours for Acid hydrolysis and cool and then add 5.0 cm^3 of 1 N NaOH for neutralization and with the diluent make up the volume. (Diluent blank solution was also prepared in same manner without MPS and disregard peaks due to blank in the test sample if any)

c)Base Hydrolysis: Take accurate quantity of about 25.00 mg of MPS in a volumetric flask of 50 cm^3 capacity. Add 5.0 cm^3 of 1 N NaOH, heat at 60 degree Celsius in water bath for 3 hours for base hydrolysis and cool and then add 5.0 cm^3 of 1N Hydrochloric acid for neutralization and with the diluent make up the volume. (Diluent blank solution was also prepared in same manner without MPS and disregard peaks due to blank in the test sample, if any)

d)Aqueous (Humidity): Take accurate quantity of about 25.00 mg of MPS in a volumetric flask of 50 cm^3 capacity. Add 5.0 cm^3 of water, heat at 60 degree Celsius in water bath for 3 hours for aqueous hydrolysis and cool and with the diluent make up the volume. (Diluent blank solution was also prepared in same manner without MPS and disregard peaks due to blank in the test sample, if any)

e)Oxidation: Take accurate quantity of about 25.00 mg of MPS in a volumetric flask of 50 cm^3 capacity. Add 5.0 cm^3 of 5 % v/v hydrogen peroxide solution, heat at 60 degree Celsius in water bath for 3 hours for Oxidation and cool and with the diluent make up the volume. (Diluent blank solution was also prepared in same manner without MPS and disregard peaks due to blank in the test sample if any)

f)Photolytic Exposure: 1.00 g MPS was exposed in photolytic stability chamber. Solution was prepared as same as parent sample.

g)Thermal Exposure: 1.00 g of MPS Batch No9025-P kept in oven at 105°C for 3.0 hrs and analyzed by HPLC. Solution was prepared as same as parent compound.

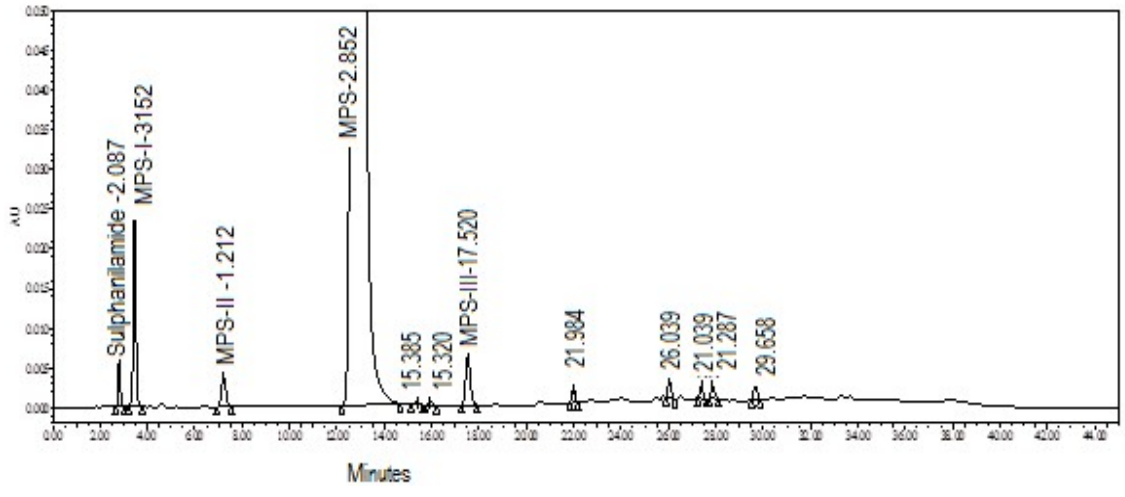

Fig. 1 MPS crude sample chromatogram

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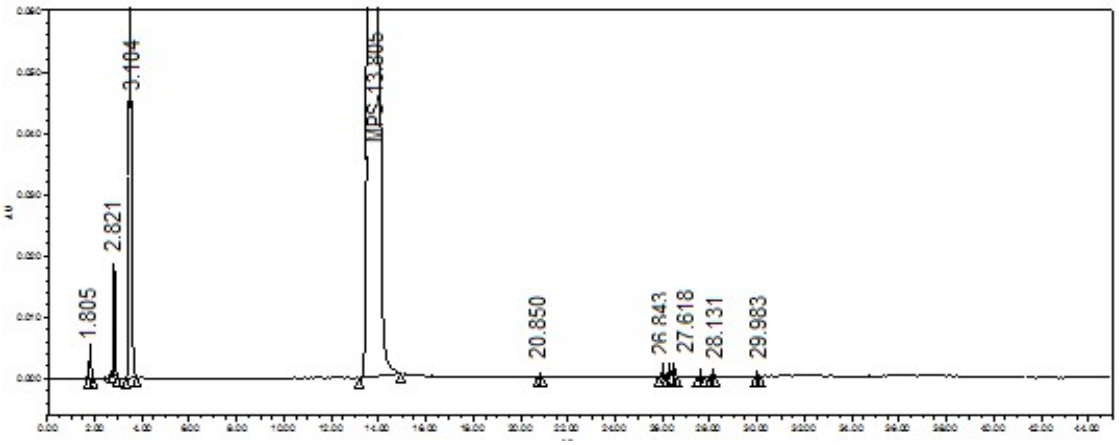

Fig. 2 Chromatogram of Acid hydrolysis of MPS under stressed condition

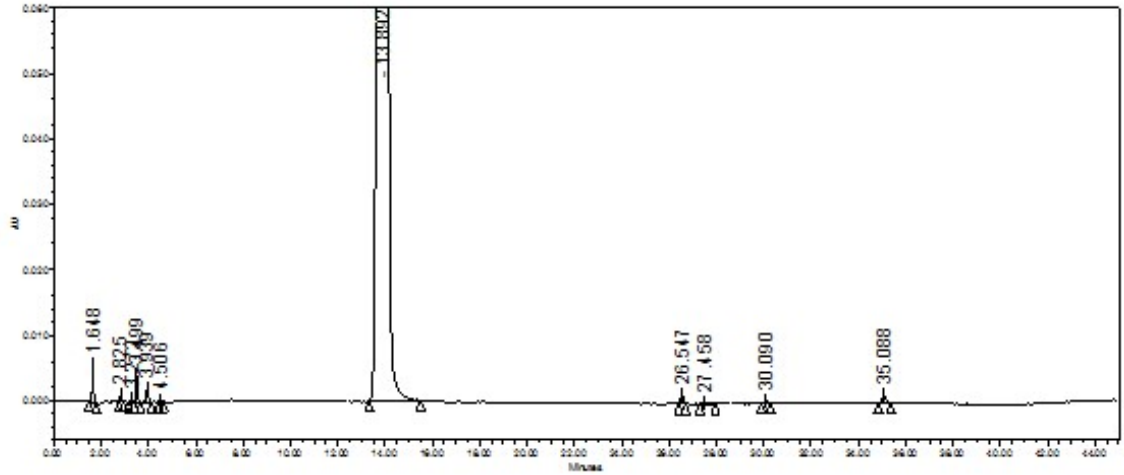

Fig. 3 Chromatogram of Base hydrolysis of MPS under stressed condition

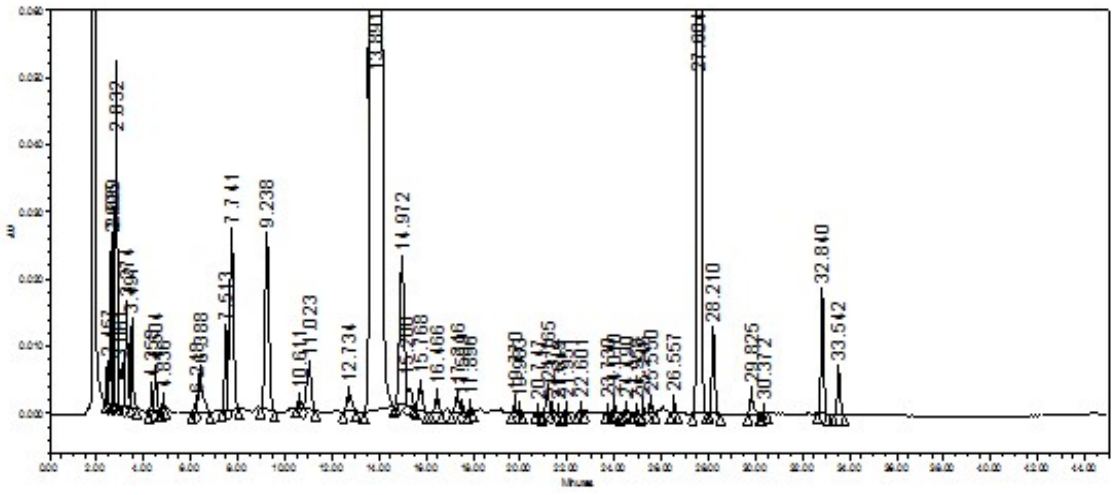

Fig. 4 Chromatogram of Oxidation of MPS under stressed condition

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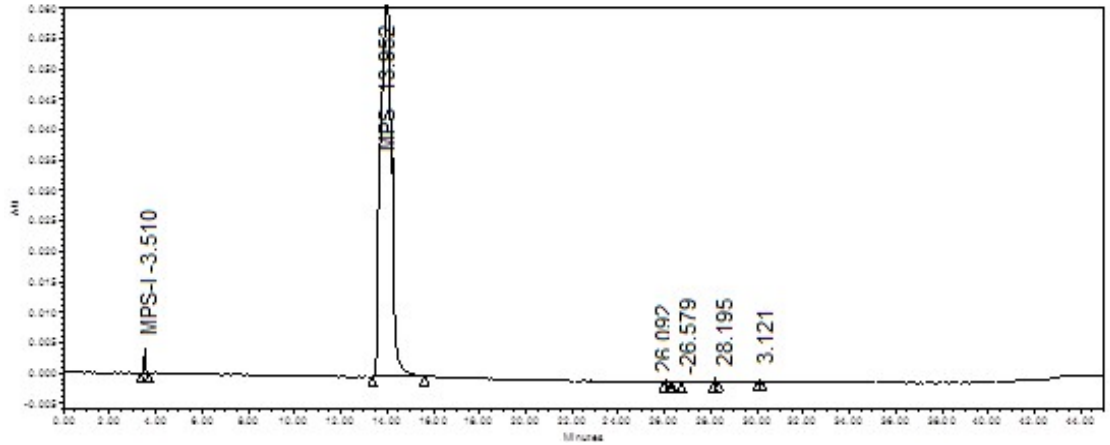

Fig. 5 Chromatogram of Aqueous (humidity) of MPS under stressed condition

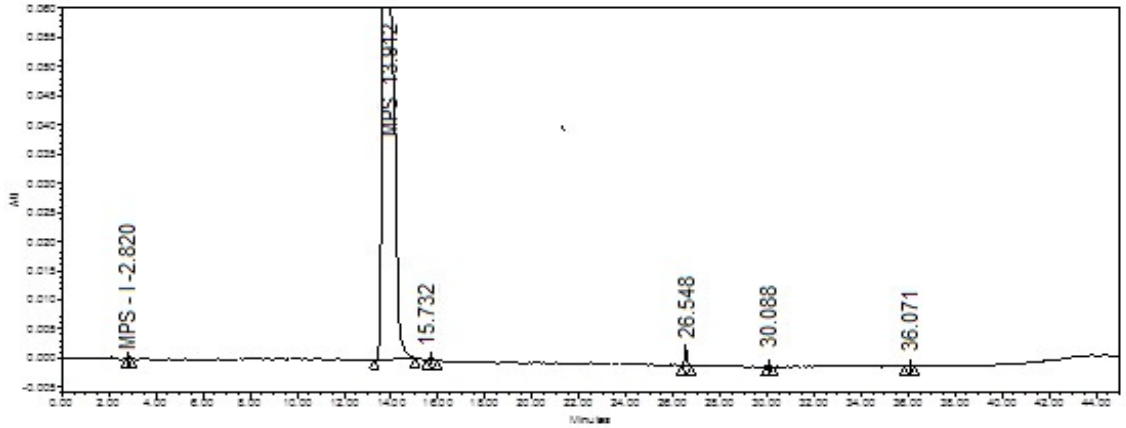

Fig. 6 Chromatogram of Photolytic Exposure of MPS under stressed condition

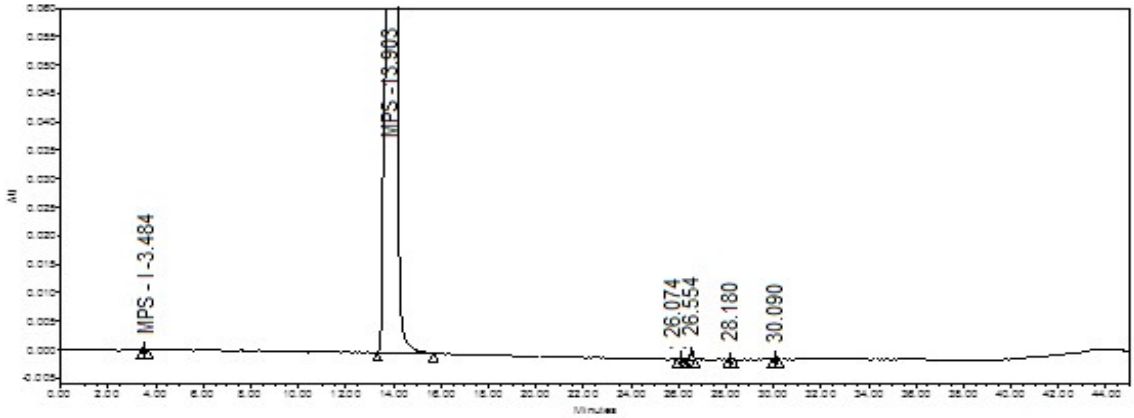

Fig. 7 Chromatogram of Thermal Exposure of MPS under stressed condition.

3. RESULTS AND DISCUSSION

Peak Purity of the principle Peak chromatographic peaks under stressed condition gave the following results:

1) Under the degradation condition, the parent sample showed five degradation impurities, 0.09% of total impurities degradation, 99.91% of MPS and PDA analysis showed the homogeneity of peak (Purity angle < Purity threshold).

2) Under the degradation condition, the aqueous hydrolysis showed five degradation impurities, 0.14% of total impurities degradation, 99.89% of MPS and PDA analysis showed the homogeneity of peak (Purity angle < Purity threshold).

3) Under the degradation condition, the acid hydrolysis showed ten degradation impurities, 5.61% of total impurities degradation, 94.40% of MPS and PDA analysis showed the homogeneity of peak (Purity angle < Purity threshold).

4) Under the degradation condition, the base hydrolysis showed ten degradation impurities, 0.40% of total impurities degradation, 99.60% of MPS and PDA analysis showed the homogeneity of peak (Purity angle < Purity threshold).

5) Under the degradation condition, the oxidation showed forty six degradation impurities, 23.09% of total impurities degradation, 76.91% of MPS and PDA analysis showed the homogeneity of peak (Purity angle < Purity threshold).

6) Under the degradation condition, the thermal exposure showed five degradation impurities, 0.09% of total impurities degradation, 99.9% of MPS and PDA analysis showed the homogeneity of peak (Purity angle < Purity threshold).

7) Under the degradation condition, the photolytic exposure showed five degradation impurities, 0.13% of total impurities degradation, 99.82% of MPS and PDA analysis showed the homogeneity of peak (Purity angle < Purity threshold).

4. CONCLUSION

Peak purity of main peak in all conditions of force degradation passes. PDA Scan for degraded drug substance and drug product is comparable to that of untreated drug substance and drug product. All peaks due to degradation are well separated from each other and from main peak. So there is no interference of blank, placebo and degradant at retention time of main peak observed in MPS drug.

This study relates that MPS-I, MPS-II, MPS, & MPS-III are well separated & comply with peak purity parameter i.e. purity angle <purity threshold.

5. ACKNOWLEDGEMENT

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