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Comparative degradation profile of biosimilar peptide Oxytocin acetate in 14 formulations versus innovator

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The WHO guideline on "Evaluation of Similar Bio-therapeutic Products (SBPs)" and recent FDA draft on "Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product" address the quality issues of biological products mainly bio-similar drugs, like proteins and peptides. Accordingly, there is a need for the generation of a comparative degradation profile of bio-similars. This includes comparison of biosimilars with the innovator to ensure their quality, safety and efficacy.

Oxytocin is a nonapeptide hormone, which is used to induce labor and to prevent postpartum hemorrhage, a major cause of maternal deaths in the developing countries. This drug is illegally used in animals to produce unnaturally large quantities of milk. Oxytocin formulations, like other peptide drug preparations, are very susceptible to degradation and require refrigeration for their storage.

The aim of this study was to compare the identity, purity, assay content, impurity profile and stability in accelerated stress conditions of 14 marketed parenteral formulations with innovator. Of the 14 products, 9 were used in humans and 5 of the use in animals. Intially comprehensive mass fragmentation pathway of the drug was established in order to characterize the degradation products. Subsequently, a validated stability-indicating profile was developed to separate the drug from degradation products. Almost all the degradation products (DPs), including some new DPs formed in 1 month and 3 month accelerated samples, were characterized using LC-MS/TOF, H/D exchange and LC-MSn studies. CD spectra were also recorded for establishing secondary structure.

The mechanistic explanation for the formation of degradation products was also given. The comparative data on amount of major degradation products after accelerated testing has been reported. In comparison to innovator, most of the formulations were not similar in terms of content, impurity and degradation profile. Except for 4 products, all others showed the same secondary structure on analysis by circular dichroism in unstressed samples. As there is no guideline in India about quality, safety and efficacy issues of bio-similars so, proper attention is definitely needed regarding their use.

Table: Comparative data of assay in formulations

Sr. No.	Name of the formulation	Pharmaceutical company	Average rplc area	Drug percentage	Rsd
1.	Oxytomed	German remedies	456950.167	103.939	10.1038746
2.	Wotocin	Wockhardt ltd.	462113.833	105.1135	4.34567018
3.	Itocin	Lupin ltd.	493863.833	112.3355	11.2315754
4.	Biotocin	Biochem	397468.333	90.40912	19.0668666
5.	Zygon	Ranbaxy	537993.167	122.3732	15.1506494
6.	Oxystar	Cadila	543214	123.5608	9.41732751
7.	Syntophar	Searle lab with canada	506470.167	115.2029	28.6761604
8.	Genox	Intas	424360.5	96.52608	19.467901
9.	Syntocinone®	Novartis	469735.2	106.8451	9.855198
10.	Brawn	Brawn labs, faridabad, india	340532.5	77.45836	17.8342952
11.	Burnet glass vials	Burnet, up, india	155942.833	35.47114	16.7071694
12.	Plastic ampoules	Haryana, india	140983.833	32.06853	39.5403092
13.	Siriram ot	Siriram laboratories, amritsar, india	439348.167	99.93521	16.4031587
14.	Up ot	Up, india	45241.5	10.29074	44.6749779
15.	Presto	Presto remedies, patiala, india	142180.833	32.3408	49.2577433
16.	Drug substance	Hemmopharma, india	439633	100%	1.60

Biography

Sheetal Sharma completed her graduation in pharmacy from Kurukshetra University, Kurukshetra, Haryana. And, she has completed her M.S. (Pharm.) degree from the Department of Pharmaceutical Analysis at the National Institute of Pharmaceutical Education and Research, S.A.S. Nagar, India.

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