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View point

Need for Extension of Real Time Stability Analysis of Drugs and Quality Control Setup in Hospitals

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ABSTRACT

Owing to the increased number issues related to medication adherence, efficacy, antimicrobial resistance, tolerance and adverse reaction with unknown ideology, few strategic approaches having been recommended and implemented in treatment procedures. Despite of these clinical oriented strategies, the success rate in eradication of many unwanted therapeutic issues quite questionable. It is believed that the existing clinical and therapeutic oriented issues pertaining the drug, it requires additional strategic implementations that nullify the probability of drug related factors. This strategy can be a drug quality control testing Centre at the hospital premises to ensure the potency and real time stabilityassessment for stability sensitive and dose sensitive drugs. Initially it may be recommended in those hospitals, which conduct clinical research, therapeutic drug monitoring, clinical evaluation of antibiotics and further it can be extrapolated based on outcome. This view invites discussion to bring a fruitful outcome rather than criticism.

Key words: Drug stability, Drugs, Hospitals, Real time testings, Stability sensitive, Quality control.

INTRODUCTION

Potency and stability of drug products or dosage forms are quality attributes to be considered as important factors that influencesthe drug potency related research outcome. In recent years, drug related issues like tolerance, resistance, adverse reactions for existing drugs are continuously increasing.[1] But those research outcomes are purely focused on either patient oriented or treatment oriented. It is known that potency, stability and impurity levels would have significant impact on the study outcome. These factors vary with time, storage condition adopted, batch, and manufacturer. In current practice, formulations employed in drug administration are based on label and expiry date assigned by the industry. In fact, the potency of the dosage form remains to the therapeutic requirement, only when appropriate storage conditions areadopted. After the implementation of ICH guidelines, the impurity levels and stability considerationsare the most important control system for quality pharmaceuticals, which directly relates the efficacy and potency in the treatment.[2]

Even in the presence of stability testing protocols in industry, many pharmaceutical products and batches have been banned and recalled in recent years. It implies that stability problems and potency deviations have been occurred at the recommended storage conditions itself. In this juncture, it is well known that many hospitals, inpatient ward; pharmacies maintain their drug products under fluctuated environments. This could trigger the stability issues in product and reduce the expected potency of medication. Apart from noncompliance of proper storage conditions, the potency variation between new products and early expiry products will have statistical significance in patient response.

This concept has been brought into discussion, exclusively for those products which are considered as degradation susceptible dosage form such as injection, infusion, dry powders etc. and for medicament which are belonging to chemical classeslike lactum, lactone, amides, ester, (which can be considered as stability sensitive drugs along with photosensitive drugs. Though health careprofessionals have adequate knowledge on stability and potency of medication, still assurance on potency and stability for those medications before introducing in clinical research always recommended for significant output.

In this context, there was a report based on the need for stability by the hospital pharmacists[3] and also a report based on stability evaluation of anticancer drugs in hospitals.[4-7] Based on these reports, it is interpreted that such studies are highly important to understand the impact of drugs potency and stability in therapeutic responses. To support the above cited view, the increased observations on 'not of quality standard (NQS) reports for drug samples by drugs control departments and magistrate issues can also be considered.[8] There were many issues on product recall by pharmaceutical companies due to stability problems too[9]

The need and extension of real time stability assessment protocol

Despite of these stability testing procedure storage and recommendations outlined by the pharmaceutical company as a compliance to reg-

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Table 1: Examples of Few drugs which are highly susceptible to degradation to be considered in Real time stability assessment

Class of drugs	Category	Expected degradation
Beta-lactum antibiotics Penicillin and cephalosporin's	Antibacterial antibiotic	Expected to hydrolyze, and produce amino and their carboxylic acids
Procaine, cinchocaine	Local anesthetics	Susceptible to hydrolysis and forms corresponding acids
Ergometrine	Used in labour	Hydrolysis to lysergic acid derivatives
Glutithimide, ethosuccinamide	anticonvulsants	Hydrolysis of imide bond
Benzodiazepine	Anticonvulsants	Hydrolyze due to moisture at low pH
Fluroquinolones(ciprofloxacin)	Antimicrobials	Photo-oxidation
Dihydropyridine(Nifedipine), Timolol, Pindolol, Propranolol	Antihypertensive	Photo-oxidation
Benzyl penicillin, Streptomycin	Antibacterial antibiotic	Photo-oxidation
Catecholamine (Adrenaline, Nor adrenaline, isoprenaline)	Adrenergic agonists	Photo-oxidation to adrenochrome derivative
Troglitazone	Antidiabetic	Photo-oxidation
Morphine	Opioids	Photo-oxidation to dimericpsudomorphine
Tetracycline	Antibacterial	Photooxidized to quinones
Chloramphenicol	Antibacterial	Photooxidized to p-nitrobenzaldehyde
Dihydropyridine(Nifedipineetc)	Antihypertensive	Photo-oxidize to aromatic pyridine
Norethisterone	Hormones	Photo-oxidize to epoxides
Promethazine, Prochlorperazine, chlorpromazine	Antipsychotics	Photo-oxidize tosulphoxides
Vitamin D	Vitamin	Photo-oxidize tosuprasterols and toxisterols
Frusemide	Diuretics	Photohydrolysis tosalumine
Folic acid	haemtonic	Oxidative deamination to pteridinecarboxaldehyde and gluamates
Nitrazepam	Sedative and hypnotics	Photoreduction to dimer derivative
Hydrochlor thiazide	Diuretics	Photon induced Dechlorination and ring opening
Diazepam	Anticonvulsant	Photon induced Conversion to benzophenones

ulatory guidelines for a particular dosage forms, only the real storage conditions employed at hospital and pharmacy sectors can determines the dug potency and safety. In connection with efficacy and safety requirement, it is also a very important concern.

The search for stability related work for drugs at hospital sectors reveled very few, relatively when compared to stability studies at industry as a part of research. But it is the need for real time analysis, by random stability study for the drug, which is stored at hospital after the transportation. Though international conference on harmonization (ICH) has considered the different climatic conditions, while implementing guidelines for stability (ICH Q1), still there is a need for real time analysis of drug after adequate exposure of drugs during transportation and storage at different conditions.

The necessity for real time stability investigation, by sampling from the market may be recommended for those drugs, which are,

- Highly susceptible to temperature
- Highly susceptible to hydrolysis in presence of moisture
- Highly susceptible to light and undergo photo-oxidation
- Producing, highly toxic impurity on storage
- Possessing narrow therapeutic window
- Responsible for drug resistance in chemotherapy
- Drug's chemical structure with imide, amide, ester, lactum, lactone, alkoxy functional groups
- Pro-drugs
- Conjugates
- There are some examples from literature[10] are listed in Table 1.

CONCLUSION

Based on the above note and observations in the current pharmaceutical health care system, it is proposed to consider for discussion and trace the reality and reliability of real-time stability assessment instability protocol as anextension to the present stability protocols. Based on the outcome, it can also bea recommendation on maintenance quality control setup in clinical research oriented hospital setup. This may nullify the drug related factors in efficacy issues, results in significant effect on quality health care system. This require lot more discussion to come out with fruitful outcome.

CONFILCTS OF INTEREST

The authors declare no conflicts of interest.

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