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# Mesoporous Silica Gel as a Formulation Aid for Moisture Sensitive Drugs and Excipients

## INTRODUCTION

Over the years, interaction of water with actives and inactive pharmaceutical materials remained thrust area for the formulation scientists to ensure production efficiency and drug stability. Although calculated water helps in formulating drug in dosage form but unwanted physical water from various sources is the cause of poor efficiency in production and instability of drug. Lactamase inhibitors like Clavulanate Potassium are highly moisture sensitive which tend to degrade in presence of water while drugs like Betahistine dihydrochloride (BHT) are highly hygroscopic which tend to liquefy if exposed to environment for 15-30min. Such a drug is very difficult to process and various operations such as mixing, transfer, granulation, compression and packing are badly affected. Externally added water can be controlled but unwanted water from humidity or hygroscopic materials (drug & excipients) has to be prevented using formulation aid like SYLOID® mesoporous silica gel for moisture protection. Its application for protecting Clavulanate Potassium is already established and results show drug is stable if premixed with SYLOID® silica(Figure 1)

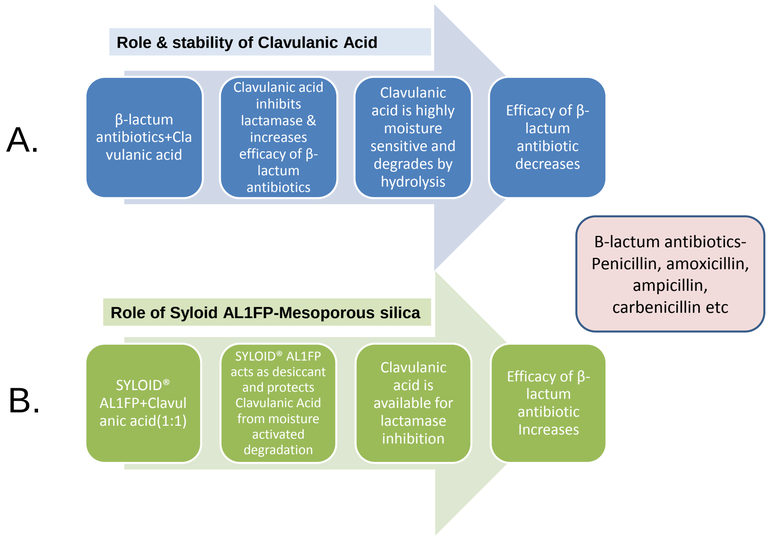


**Figure 1.** **A.** Clavulanic Acid role in increasing effectiveness of β-lactum antibiotics and its susceptibility to moisture degradation
**B.** Utilizing SYLOID® AL-1FP silica to protect Clavulanic Acid from moisture-activated degradation

Highly crowded silanol groups, high surface area of 700$m^2$/g and strong adsorption capacity with capillary forces of SYLOID® AL-1FP silica played major role to absorb and stabilize unwanted water.

Similar to drugs, hygroscopic excipients also affects the various manufacturing processes. Poly Vinyl Pyrrolidone (PVP) is preferred binder in tablet formulation. Due to its hygroscopic nature processes like powder mixing, weight variations content uniformity, and compression are influenced. Hence, we studied both BHT and PVP K 30 as examples of hygroscopic compounds and premixed with silica to address the issue.

## OBJECTIVE

The objective of the current research work is to study the effects of different porosity mesoporous silicas on the moisture stabilization of different drugs and excipients.

## EXPERIMENTAL

### Materials

BHT as a model moisture sensitive drug was purchased from Enal Drugs Pvt Ltd, India. PVP K 30 was obtained from SRL chem. Mesoporous silica used was SYLOID® silica manufactured by W.R.Grace & Co. All the other chemicals and solvents were AR grade from leading manufacturers**.**

### Methods

BHT and PVP K 30 were mixed physically with SYLOID® silica in 1:1 ratio individually. BHT being highly hygroscopic get liquefied in 1hour if kept open at room temperature(RT-60%RH, 25°C). Hence, BHT is selected as model drug to claim applications of mesoporous silica gel in stabilization of moisture sensitive drug. Analytical method for BHT was developed and % purity of drug was determined by HPLC. The mixed powder sample and individual PVP K 30 were kept at accelerated humidity (75%RH) and temperature (40°C) in stability chamber. BHT and mixed BHT+SYLOID® silica were kept at RT. The visual observations were recorded. Tablets of BHT with and without SYLOID® 244FP silcia were prepared and observations like weight uniformity, content uniformity and hardness of tablets were recorded.

## RESULTS AND DISCUSSION

The % purity for BHT was found to be 99.76 by HPLC method. Over the period, alone PVP K 30 and BHT were converted to liquid form due to their highly hygroscopic nature (Figure 2). However, samples kept with SYLOID® silica were found to be in the powder form. The flow properties of silica mixed samples were comparable with initial samples. Manufacturing operations like mixing and compression were improved. High surface area ensured water molecules are bound with silanol groups in monolayer and become unavailable to react with drug/additives. This results in increased productivity as well as stability of moisture sensitive drugs like BHT and excipients like PVP K 30.

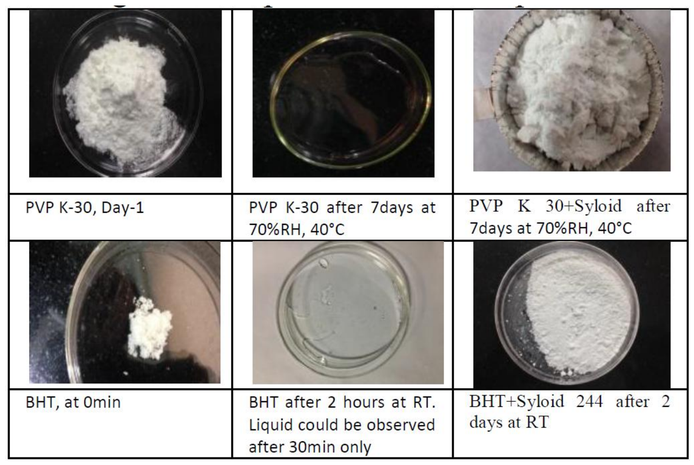


**Figure 2.** Physical observations of PVP K 30 and BHT stability samples

SYLOID® 244FP silica improved the weight and content uniformity, and hardness of tablets while tablets prepared without silica failed in all these parameters. Large particle SYLOID® XDP silica was not as effective in improving these parameters(Figure 3). The particle size (XDP=50 micron vs. 244FP=5 micron) is the principle difference between the two silicas.

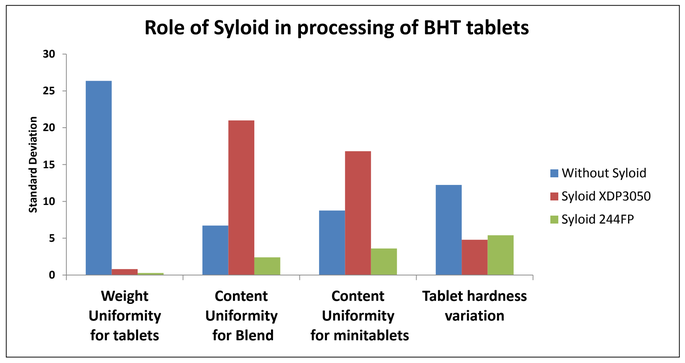


**Figure 3.** Effect of SYLOID® 244FP on tabletting

The dissolution of BHT tablets prepared with SYLOID® silica shows 100% release in aprox.1.5hr (Figure 4). The faster release of SYLOID® 244FP can be attributed to its small particle size

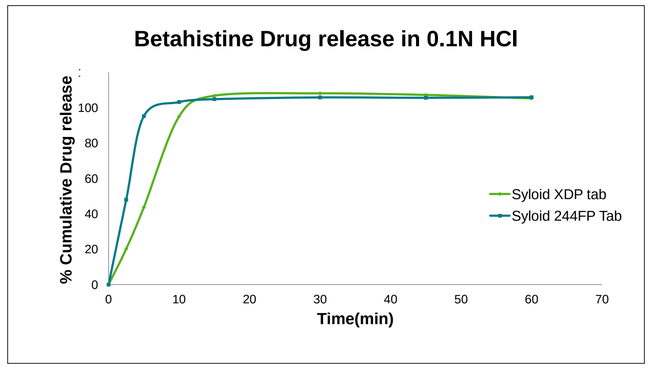


**Figure 4. :** Dissolution of BHT tablets prepared with SYLOID® silica

## CONCLUSIONS

SYLOID® Mesoporous silica gels are highly porous and with high surface area, can protect hygroscopic compounds from moisture and increases drug stability and processability in solid dosage form manufacturing. Mesoporous silicas in general and SYLOID® silicas in particular can be an effective and useful formulation aid for formulations containing moisture sensitive drugs and excipients.

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