NEW ADSORBERS FOR THE REMOVAL OF GENOTOXIC IMPURITIES FROM ACTIVE PHARMACEUTICAL INGREDIENTS

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Active pharmaceutical ingredients (APIs) available in the market are mostly synthesized, in organic solvent media, using highly reactive molecules that may be present in the final product as genotoxic impurities (GTIs). These compounds have the ability to react with DNA, preventing its normal replication, resulting in an associated carcinogenic risk, becoming an increasing concern from pharmaceutical companies and regulatory authorities [1]. Although it is desirable to avoid the use of GTIs in the manufacture of APIs, this is not always possible. Therefore, there is a call to develop simple, robust and economical routes to remove GTIs to limits below the Threshold of Toxicological Concern (1.5 µg/day) [2]. Such adsorbents should be highly selective to reach ultra-low GTI levels with minimal API losses and compatible with organic solvents where the API synthesis takes place [3].

Herein we report two different strategies for the development of new adsorbing materials designed for selective removal of GTIs from API organic solvent solutions. These new materials are: i) molecular imprinted polymers (MIPs), in the particular case designed for removal of an aromatic amine GTI, 4-dimethylaminopyridine) [4]; and ii) a novel functionalized polymer consisting on polybenzimidazole (PBI) modified with a DNA base (PBI-adenine). PBI-Adenine is designed to have a high affinity for a broad range of DNA alkylating agents mimicking the DNA-GTI adduct formation that takes place in vivo [5,6]. These platforms proved to be robust materials being able to remove, in a single stage, more than 95% of the GTIs from organic solvent API mixtures. Both approaches, meet the pharmaceutical industry challenges, by opening new horizons for the use of these adsorbers as a complement to the existing operation units as MIPs, as well as their assembling as membranes for organic solvent nanofiltration (OSN) derived from PBI.

References

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