

Functionalized Calixarenes Drug-Sensing Receptor: A Review

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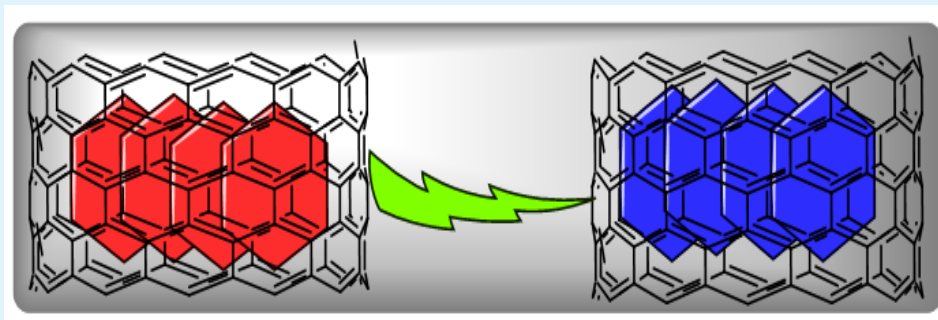
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Abstract

This review gives a comprehensive insight on the functionalized calixarenes in the field of drug sensing. The spectacular feature of calixarenes with three-dimensional surface makes it capable as sensor for a drug. Under the calixarene scaffold, there are reports on different sensing applications which include calixarene functionalized nanoparticles, drug interactions which are also reviewed in this article. Herein, a brief survey is presented which includes sensing of toxic heavy metal ion, molecules and drugs interactions.



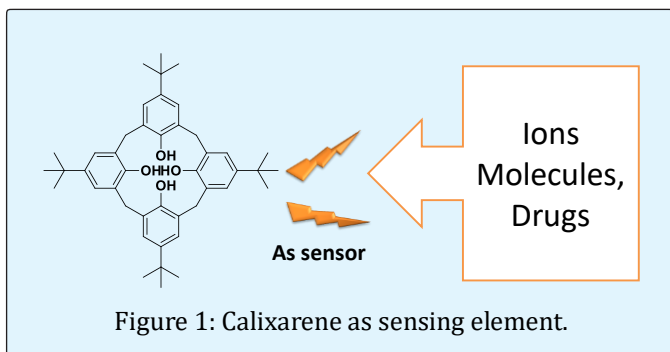
Keywords: Sensor, calix system, Metal ions, Drug interaction.

Introduction

Calixarenes have been first introduced by Gutsche D in 1978 [1]. The word “calix” means a vase and the word “arene” refers to any aromatic building unit. Structurally, calixarenes possess an upper rim, middle annulus and a lower rim. According to reports, functionalized calixarenes includes crown and fullerene-bearing calixarenes, bridged calixarenes, polymeric calixarenes, modified calixarenes, and hetero-and hetero-calixarenes [2]. Calixarenes can be chosen as efficient sensor because

of its chemical stability, selective complexation ability and low toxicity properties [3,4]. Due to their unlimited functionalization properties, calixarene functionalized nanoparticles are also reported to act as selective sensors for different ions and molecules [5]. The interaction and administration of drug molecules to the body requires them to be framed into a suitable dosage form that may be dictated by the fundamental properties of the drug or the site of the drug target delivery and disease being treated [6]. Drug solubilization and delivery using calix [n]arene aggregates or calyx [n] arenes that have been

assembled into or form part of larger supramolecular structures has been reported [7].



The basic principle of functionalized calixarenes to act as sensor lies behind any changes or tracking any kind of signal detection in its environment. The complexation behaviour of metal cations and molecules with calix [4] resorcinarene was studied by spectrophotometry and spectrofluorometry [8,9]. The use of functionalized oxacalixarene as a fluorescent sensor for the selective and sensitive detection of ions like copper and cerium and molecules like pendimethalin has also been reported [10,11]. Different thiacalixarene derivatives have also been explored for the detection of mercury and cobalt ion based on fluorescence mechanism [12,13]. An ionophore based on schiff-based calixarene has been used for sensor Ag (I) ions [14]. Threat agents like nitro aromatic compounds have also been selectively sensed by Dipyrenylcalix [4] arene [15]. Sensing and recognition of commercially pertinent molecules is ongoing research processes that ubiquitously play roles in biological, medical, environmental, and chemical sciences [16]. With calixarene, it's possible to tailor the complementary structural components with optimal recognition property between the host and guest. Given the spatial distribution and multitude of potential binding site provided by the calixarene, it can allow the rational control of the binding properties. The fact that both the upper and lower rims of the expanded or extended calixarene can be functionalized; it successively tailors pre organized supramolecular architecture for flanking the chemical analytes in the binding sites. Among the binding forces, non-covalent interactions including hydrogen-bonding and weak van der Waal interactions are particularly useful. The calixarene receptors comprising the functional groups such as amides, ureas, anthracene, thiourea, quinoline, etc enable the calixarenes to selectively bind the specified analytes via non-covalent interactions. Other than experimental platforms to perform such chemical sensing, state-of-art computational methods are

nowadays used. Urea and thiourea substituted calixarene has been inspected by the Density Functional Theory (DFT) method to prioritize the binding selectivity among an array of spherical and linear anions [17]. Of special interest are the luminescent properties of some of the functionalized calixarene (chromophore or fluorophore) which allow the visual handing and commercial ease of such framework. Upon binding with a guest, the change of the spectral properties would give rise to a sensing mechanism. Using dispersion corrected DFT and Kohn-Sham molecular orbital theory, Ortolan, et al. explored the role of physical factors that affect the noncovalent interactions in anion sensing on calixarene. They report that the strength of the host-guest interaction can be enhanced through the introduction of strongly electron-withdrawing groups, triazine units and coordination of a metal to the arene rings [18]. Murphy et al has used the DFT to investigate the effect of methylation of the lower-rim tetraphenolic pocket of calyx [4] arene on the binding of small gaseous molecules such as H₂, O₂, N₂, H₂O, CO₂, NH₃, H₂S, N₂O, HCN, and SO₂ [19]. Moreover, DFT-Grimme's dispersion correction-Becke-Johnson damping functions (D3BJ) scheme was applied the unveil the mechanistic insights the recognition of anions by the electron deficient cavity using the heterocalixarene rings [20].

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