Chemical Analysis of *Zingiber* Species from Bangladesh and Improvement of the Solubility of Zerumbone, A Multifunctional Compound, by Cyclodextrins

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People have been using medicinal plants as a traditional medicine, a rationale herbal drug or as a source of therapeutically pure compounds. They have also contributed as a potential source for the discovery and development of natural product based modern drugs. With the increasing prevalence of life style related diseases, the demand of natural products specially plant derived drugs are rising. In the present research work, I performed the chemical analysis of three *Zingiber* species from Bangladesh *i.e.* *Zingiber salarkhanii* Rahman et Yusuf, *Zingiber rubens* Roxb and *Zingiber montanum* (J. Koenig) Link ex A. Dietr, also I improved the solubility property of a bioactive compound named zerumbone by cyclodextrins.

*Zingiber salarkhanii* is a newly reported species from Bangladesh, locally it is known as “Tara-gach”. The rhizome juice of *Z. salarkhanii* is used for the treatment of gastric pain. In present research, the dried ethanol extract (ZS) was suspended in water and partitioned with hexane to give hexane soluble (ZSH) and water soluble (ZSW) fractions. The hexane soluble fraction was further purified by various column chromatographic methods to obtain four compounds *i.e.* 5-hydroxy-3,7-dimethoxyflavone (1), β-sitosterol (2), stigmasterol (3) and oleic acid (4).

*Zingiber rubens* is locally known as “Murga-gach”. Rhizome is used in traditional medicine for the treatment of common cold, lipoma and piles. The dried ethanol extract (ZR) was suspended in water and partitioned successively by hexane and ethyl acetate to give hexane soluble (ZRH), ethyl acetate soluble (ZRE) and water soluble (ZRW) fractions. These fractions were further purified by various column chromatographic methods to obtain three compounds *i.e.* β-sitosterol (2), iso-serratol (5) and methyl linoleate (6).

*Zingiber montanum* is locally known as “Bon ada” and fresh rhizome juice is consumed as a healthy drink. Rhizome of *Z. montanum* is used in traditional medicine for treating bloating, constipation, dyspepsia, flatulence, gastritis and so on. The dried ethanol extract (ZM) was suspended in water and partitioned with hexane to give hexane soluble (ZMH) and water soluble (ZMW) fractions. The dried fractionated extracts were subjected to various column chromatographic methods to obtain six pure compounds *i.e.* zerumbone (7), kaempferol 3-O-methyl ether (8), kaempferol 3-O-α-rhamnopyranoside (9), kaempferol 3-O-α-(4”-O-acetyl) rhamnopyranoside (10), kaempferol 3-O-α-(3”-O-acetyl) rhamnopyranoside (11) and kaempferol 3-O-α-(3”, 4”-di-O-acetyl) rhamnopyranoside (12). Except zerumbone (7) all are isolated for the first time from *Z. montanum*.
Chart 1. Structures of compounds isolated from Z. salarkhani, Z. rubens and Z. montanum

The monocyclic sesquiterpene zerumbone has promising biological activities such as antioxidant, anti-inflammatory, anticancer. To be used as a pharmaceutical preparation it has some disadvantages like solubility, stability, bioavailability and so on. Thus, utilization of this sesquiterpene in food and pharmaceutical industries could be improved by the formation of inclusion complexes with cyclodextrin (CyD). So, as an earlier stage of drug development, my focus was to increase the water solubility and stability of zerumbone by using 2-hydroxypropyl-β-cyclodextrin (HP-β-CyD) & sulfobutylether-β-cyclodextrin sodium salt (SBE-β-CyD). The phase solubility diagram showed $A_L$ type, suggesting 1:1 inclusion complex between CyD and zerumbone, whereas SBE-β-CyD ($755 \text{ M}^{-1}$) indicating higher solubilizing effect compare to HP-β-CyD ($255.3 \text{ M}^{-1}$). To make sure the complexation between CyDs and zerumbone in the solid-state differential scanning calorimetry (DSC), X-ray diffractometry (XRD) was also performed.

The results obtained in this study indicated that, dried rhizome of Z. montanum contains high amount of zerumbone. So, this Bangladeshi ginger can be a remarkable source for zerumbone. Further studies should focus on the analysis of biological activity of reported bioactive compounds, to establish the mechanism of action and the stoichiometry analysis of the liquid inclusion complexes of zerumbone-cyclodextrins and in-vivo evaluation of this complexes to provide sufficient evidence to be used as a pharmaceutical preparation in future.