



Fig. 26 Occurrence of the quinazolinone privileged scaffold (indicated in red) within the drugs Etaqualone (**43**, sedative), Mecloqualone (**44**, sedative), and Nolatrexed (**45**, antineoplastic) and the natural products Tryptanthrin (**46**, antiparasitic, found in various plants), Aurantiamide A (**47**, cytotoxic, isolated from *Penicillium aurantiogriseum*), and (–)-Circumdatin H (**48**, mitochondrial respiratory chain inhibitor, isolated from *Aspergillus ochraceus*)

A (CCK A), which is associated with gastrointestinal cancer (Evans et al. 1988). Combinatorial synthesis of a library of benzodiazepines by the Ellman group then led to the identification of a selective CCK A antagonist, Bz-423 (**42**, Bunin et al. 1994; Boitano et al. 2003).

It was then soon realized that many of such privileged structures appear across various drugs and natural products, often within completely different therapeutic areas. Various approaches such as NMR-based target binding analysis (Hajduk et al. 2000) and cheminformatics analysis of the CRC Dictionary of National Products (Koch et al. 2005) have led to a large list of privileged scaffolds, and it is likely that there are much more privileged structures out there that have not been identified yet. An extensive list of privileged structure prevalence was collected by Welsch and co-workers, of which a small part is shown in Fig. 26 to illustrate the concept (Welsch et al. 2010). Important to note is that the quinazolinone motive does not only have different targets but is also incorporated into natural products synthesized by completely different organisms. Of course, one could wonder why privileged structures have the ability to bind multiple targets and why nature makes frequent use of the same motives to synthesize natural products. This can be explained by the fact that, while there are a vast amount of proteins known, the types of structural features or folds that they incorporate are rather limited, resulting in similar binding sites even when the similarity of two proteins is not immediately obvious (Breinbauer et al. 2002). This similarity also implies that natural systems are likely to use similar strategies, e.g., for cellular signaling processes, defense against predators, and others (Welsch et al. 2010).