Saudi Pharmaceutical Journal (2014) **22**, 1–2

King Saud University

**Saudi Pharmaceutical Journal**

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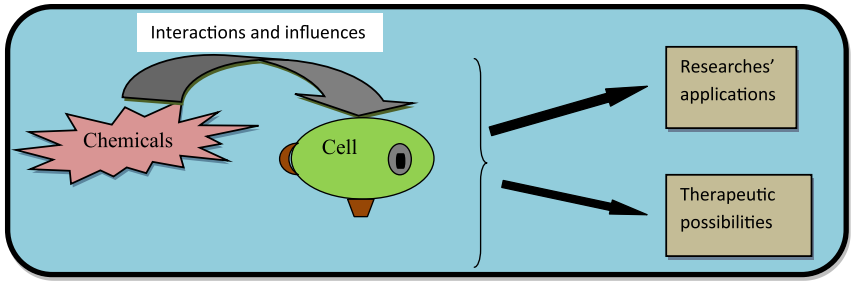
EDITORIAL

# Biological properties and perspective applications of "Bio-neuter" chemicals?




Among the different cell constituents, a huge number of modern researches, both in biology and pharmacology, focus on the cell receptors as a key element in bio-communication and signal transduction within the *in vivo* system. These receptors constitute the main target for the modern pharmacotherapy thus; have been the topic of many researches in many fields including pharmacology, physiology, neurology and toxicology. Herein, the main general principle remains the interactions between different chemicals and both the cell receptors (in addition of the related pathways) and the DNA resulting in many applications in diverse fields including pharmacology (drugs), toxicology (anti-poison), medical diagnoses...

On the other hand, divers chemicals constitute research materials rather than agents that are supposed to have an effect on the cell. Indeed, chemicals such as reagents, solvents, and kit's solutions are typical examples of agents that are used with biological matters (Cell, organs and organism) when laboratories researches are carried out. During those experiments, such agents are supposed to neither interfere with the assay procedures nor to influence the results by modifying the cell properties, exactly like excipients that enter in the composition of medicines are pharmacologically inactive.

Peer review under responsibility of King Saud University.

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However, new evidences are pointing out some exceptions about those agents supposed "bio-neuter". Indeed, some chemicals including reagents and solvent have been shown to influence the biology or the physiology of the cells which means that they are not "bio-neuter". For example chemicals that influence the cell viability might influence the test of Alamar Blue and thus, cannot be included in an assay medium in which cell viability or a related parameter is evaluated. On the other hand, this same property can be "pharmacologically exploited" to develop new drugs that could be efficient in degenerative diseases.

Some consequences of the interactions between G protein coupled receptors (GPCRs) and Dimethyl sulfoxide (DMSO) represent a good illustration of the concepts that are introduced within this commentary. Indeed, the increased pharmacological importance of the GPCRs family among, mainly but not only, the medical therapies has led to a high amount of research on those receptors and the usage of different chemical reagents or additives has been shown, in some cases, to influence GPCR's biological status. Herein, we illustrate how DMSO, which if used at a low proportion within the media is known (from an experimental viewpoints, at least) not to affect the cell interactions and properties, can have important influences from which we can take benefits in researches fields. In neurobiology DMSO constitutes an amphiphilic compound with the ability to scavenge hydroxyl radicals thus; DMSO can be used to develop molecules with antioxidant neuroprotective properties (Sanmartin-Suarez et al., 2011). In addition, a


http://dx.doi.org/10.1016/j.jsps.2013.01.006

DMSO's versatile effect has been shown for the expression of GPCRs in the methylotrophic yeast P. pastoris (Andre et al., 2006). Furthermore, adding DMSO to baby hamster kidney (BHK) cell cultures that express neuromedin U (Shukla et al., 2007) (Xia et al., 2008) or bradykinin receptors (Shukla et al., 2006) resulted in a 5- to 6-fold increase of the functional expression of these receptors. To estimate the effect of DMSO exposure on GPCR expression in Chinese hamster cells, expressing μ - and κ opioid receptors and neuropeptide FF (NPFF) receptors (NPFF1 and NPFF2), assays were carried out and a significant increase in functional expression levels was observed for Mu (μ), kappa (κ) and NPFF2 receptors but not for NPFF1 receptors, whereas, this treatment did not modify the affinity (Kd) of the receptors. This study's importance lies in the fact that opioid modulating systems include NPFF1 and NPFF2 (Mollereau et al., 2005) pain perception, Mu ( μ) and kappa ( κ), delta ( δ) receptors and opioid receptor-like1 (ORL1) constitute the four main classes of opioid receptors involved in this physiological process. In conclusion, DMSO does not affect the GPCR expression level of all receptors showing the selectivity such chemicals can have which will turn out to be a pharmacological specificity in drug development. However, the information we have about the potential effects may provide further details to obtain more pharmacological data or to study functional solubilization and folding (Talmont et al., 2010) of receptors.

Importantly, based on the structural similarities that exist between different GPCRs we can predict similar properties and interactions for others GPCRs as a result of the interaction with agents like DMSO or chemical agents that have either analogies with DMSO or have been shown with similar properties.

Such data could be important. Indeed, studying new elements about GPCRs system, and eventually other receptors and pathways, will surely lead to interesting findings about how to obtain cells and animals with modified receptors and that can be used to carry out new assays to further investigate GPCR's properties, both in vitro and using animal models (Talmont et al., 2012), via increasing receptor's expression. Importantly, we draw attention to the DMSO antioxidant properties that may provide starting points to develop neuroprotective drugs using a kind of "chemically modified DMSO" or other molecules that have similar properties. Especially new factors have been pointed to influence some GPCRs receptors activity (Ghanemi, He, and Yan, 2013).

More attention should be paid to chemicals widely used in laboratories such as Ethylenediaminetetraacetic acid (EDTA) and the ingredient of the cell culture's medium which are in direct, and continuous, contact with the cells and thus, are more likely to influence the cell development-related properties.

By extrapolating to other chemicals, we would suggest that further investigation, especially those that will take into consideration data from different laboratories reporting effects of chemicals on cells, will lead to new advances and applications. I hope this editorial will draw more attention to this aspect on the potential interaction between chemistry and biology and as a result contribute to develop new therapies, design better laboratory protocols and optimize laboratory assays.

## Financial disclosures and declaration of Interest

The author declares that there are no financial interests or conflicts of interest.

## References

Andre, N., Cherouati, N., Prual, C., Steffan, T., Zeder-Lutz, G., Magnin, T., Pattus, F., Michel, H., Wagner, R., Reinhart, C., 2006. Enhancing functional production of G protein-coupled receptors in *Pichia pastoris* to levels required for structural studies via a single expression screen. Protein Sci. 15 (5), 1115–1126.

Ghanemi, A., He, L., Yan, M., 2013. New factors influencing G protein coupled receptor's system functions. Alexandria J. of Med. 49 (1), 1–5.

Mollereau, C., Roumy, M., Zajac, J.M., 2005. Opioid-modulating peptides: mechanisms of action. Curr. Top Med. Chem. 5 (3), 341–355.

Sanmartin-Suarez, C., Soto-Otero, R., Sanchez-Sellero, I., Mendez-Alvarez, E., 2011. Antioxidant properties of dimethyl sulfoxide and its viability as a solvent in the evaluation of neuroprotective antioxidants. J. Pharmacol. Toxicol. Methods 63 (2), 209–215.

Shukla, A.K., Haase, W., Reinhart, C., Michel, H., 2007. Heterologous expression and comparative characterization of the human neuromedin U subtype II receptor using the methylotrophic yeast *Pichia pastoris* and mammalian cells. Int. J. Biochem. Cell Biol. 39 (5), 931–942.

Shukla, A.K., Reinhart, C., Michel, H., 2006. Dimethylsulphoxide as a tool to increase functional expression of heterologously produced GPCRs in mammalian cells. FEBS Lett. 580 (17), 4261–4265.

Talmont, F., Mollereau, C., Muller, I., Zajac, J.M., 2010. Solubilization and functional reconstitution of human neuropeptide FF2 receptors. Anal. Biochem. 398 (2), 225–229.

Talmont, F., Mollereau, C., Zajac, J.M., 2012. Expression of opioid and anti-opioid receptors in Chinese hamster ovary cells after exposure to dimethyl sulfoxide. Anal. Biochem. 420 (1), 99–100.

Xia, H., Liu, L., Reinhart, C., Michel, H., 2008. Heterologous expression of human Neuromedin U receptor 1 and its subsequent solubilization and purification. Biochim. Biophys. Acta 1778 (10), 2203–2209.

Abdelaziz Ghanemi *

*Department of Pharmacology, China Pharmaceutical University, No. 24 Tong Jia Xiang, Nanjing 210009, Jiangsu Province, People's Republic of China*

*Department of Pharmacy, Faculty of Medicine, Mentouri-Constantine University, Constantine 25000, Algeria*
*Mobile: +8613776688144.*
*E-mail address:* ghanemiabdelaziz@hotmail.com