



QUANTUM ANALYSIS OF THE INTERACTION OF SALBUTAMOL AND NT

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ABSTRACT

Salbutamol (SB) is a beta-adrenergic stimulant that has particular action on beta-2-adrenergic receptors (β 2ARs). Patients report improvement in their condition after SB consumption. The SB improves lung function in healthy humans. Although, its use has systemic cardiovascular effects and elevation of blood pressure. Bronchodilator drugs are widely used therapeutic agents for the treatment of asthma and chronic obstructive pulmonary disease (COPD). COPD and asthma are two highly prevalent inflammatory diseases characterized by airflow obstruction. The objective of this work was to investigate how the SB interacts with the neurotransmitters (NT). We used the quantum semi-empirical parametric method 3 (SE-PM3) for Bandgap (BG), electrostatic potential (EP) and electron transfer coefficient (ETC, adimensionless) calculations. We used the HyperChem molecular simulator for

Windows Serial # 12-800-1501800080 SE-PM3 to extract the molecules. Serotonin is the one with whom the SB most interacts with all NTs. We also found that SB does not interact as an antioxidant in NTs and that SB has less affinity with noradrenaline.

KEYWORDS: Salbutamol, Neurotransmitters, SE-PM3, β 2ARs receptors.

INTRODUCTION

The SB is a beta-adrenergic stimulant that has particular action on β 2ARs.^[1,2] Patients report improvement in their condition after SB consumption.^[3] The SB improves lung function in healthy humans.^[4] Although, its use has systemic cardiovascular effects and elevation of blood pressure.^[5] This is available in a variety of dosage forms such as injections, tablets, syrups, aerosols, and nebulizers.^[1]

The SB has metabolic effects: Increased glycogenolysis in the liver and skeletal muscle. Increased lipolysis in adipose tissue, increased free fatty acid in plasma and ketone. The release of insulin.^[6-9] Researchers have shown that after the use of SB the concentrations of polyhydroxybutyric acid, lactate, aconitate, 5 - hydroxyindoleacetic acid (5-HIAA), taurine, glucose, cis-aconitate, deoxyadenosine and 2 - aminoadipate are increased.^[6,10]

The enteroendocrine cells collectively constitute our largest endocrine tissue, enterochromaffin (EC) cells are the most important they secrete serotonin (5-HT).^[11] Exogenous 5-HT significantly attenuates the thermogenic potential of the β -adrenergic agonist receptor.^[12]

Bronchodilator drugs are widely used therapeutic agents for the treatment of asthma and COPD.^[13,14] The standard treatment of acute severe asthma is the use of short-acting inhaled agonists (SB), systemic corticosteroids and supplemental oxygen.^[15,16]

COPD and asthma are two highly prevalent inflammatory diseases characterized by airflow obstruction.^[17] Patients experience several different symptoms, such as dyspnea, wheezing, and tightness in the chest.^[18] Of all the symptoms of COPD, dyspnea is the most dominant and determinant.^[19,20]

Doctors have located the β 2ARs throughout the body including the airways and alveolar cells. β 2ARs regulate the elimination of lung fluid through a variety of mechanisms, including ionic transport in alveolar cells and relaxation of lung lymphatics.^[4]

The objective of this work was to investigate how the SB interacts with the NT. We used the SE-PM3 for BG, EP, and ETC.

METHODOLOGY

SE-PM3 is a molecular modeling program used by scientists to analyze the quantum composition of molecules and to obtain HOMO-LUMO, BG, EP and other properties. We use the data to calculate ETCs.^[21-25]

We used the HyperChem molecular simulator for Windows Serial # 12-800-1501800080 SE-PM3 to extract the molecules.

Table: 1 Parameters used for quantum computing molecular orbitals - HOMO and LUMO.^[26]

Parameter	Value	Parameter	Value
Total charge	0	Polarizability	Not
Spin Multiplicity	1	Geometry Optimization algorithm	Polak-Ribiere (Conjugate Gradient)
Spin Pairing	RHF	Termination condition RMS gradient of	0.1 Kcal/Amol
State Lowest Convergent Limit	0.01	Termination condition or	195 maximum cycles
Interaction Limit	50	Termination condition or	In vacuo
Accelerate Convergence	Yes	Screen refresh period	1 cycle

Table: 2. Parameters used to visualize the map of the electrostatic potential of the molecules.^[26]

Parameter	value	Parameter	Value
Molecular Property	Property Electrostatic Potential	Contour Grid increment	0.05
Representation	3D Mapped Isosurface	Mapped Function Options	Default
Isosurface Grid: Grid Mesh Size	Coarse	Transparency level	A criteria
Isosurface Grid: Grid Layout	Default	Isosurface Rendering: Total charge density contour value	0.015
Contour Grid: Starting Value	Default	Rendering Wire Mesh	

RESULTS AND DISCUSSION

The table 3. shows the ETCs values calculated from the SB and NT interaction. In this one can observe how the SB does not act as an antioxidant of the NT. The highest ETC recorded was SB: NE, therefore, its affinity is considered to be very low. The lowest recorded ETC is SB: Adrenaline.

Table: 3. SB: NT Cross Bands

Reducing Agent	Oxidizing Agent	Homo	Lumo	BG	E-	E+	EP	ETC
SALBUTAMOL	SALBUTAMOL	-9.103028	0.05508098	9.15810898	-0.102	0.187	0.289	31.68895841
SALBUTAMOL	ADRENALIN	-9.103028	0.09176242	9.19479042	-0.102	0.198	0.3	30.6493014
SALBUTAMOL	SEROTONIN	-9.103028	-0.1294475	8.9735805	-0.102	0.141	0.243	36.92831481
SALBUTAMOL	DOPAMINE	-9.103028	0.1988791	9.3019071	-0.102	0.189	0.291	31.96531649
SALBUTAMOL	GABA	-9.103028	0.9385893	10.0416173	-0.102	0.18	0.282	35.60857199
SALBUTAMOL	GLYCINE	-9.103028	0.8744405	9.9774685	-0.102	0.188	0.29	34.40506379
SALBUTAMOL	ASPARTY ACID	-9.103028	0.5161864	9.6192144	-0.102	0.198	0.3	32.064048
SALBUTAMOL	GLUTAMIC ACID	-9.103028	0.5371279	9.6401559	-0.102	0.197	0.299	32.24132408
SALBUTAMOL	NORADRENALINE	-9.103028	-0.00427538	9.09875262	-0.102	-0.222	0.12	75.8229385
SALBUTAMOL	ACETYLCHOLINE	-9.103028	1.034277	10.137305	-0.102	0.105	0.207	48.97248792

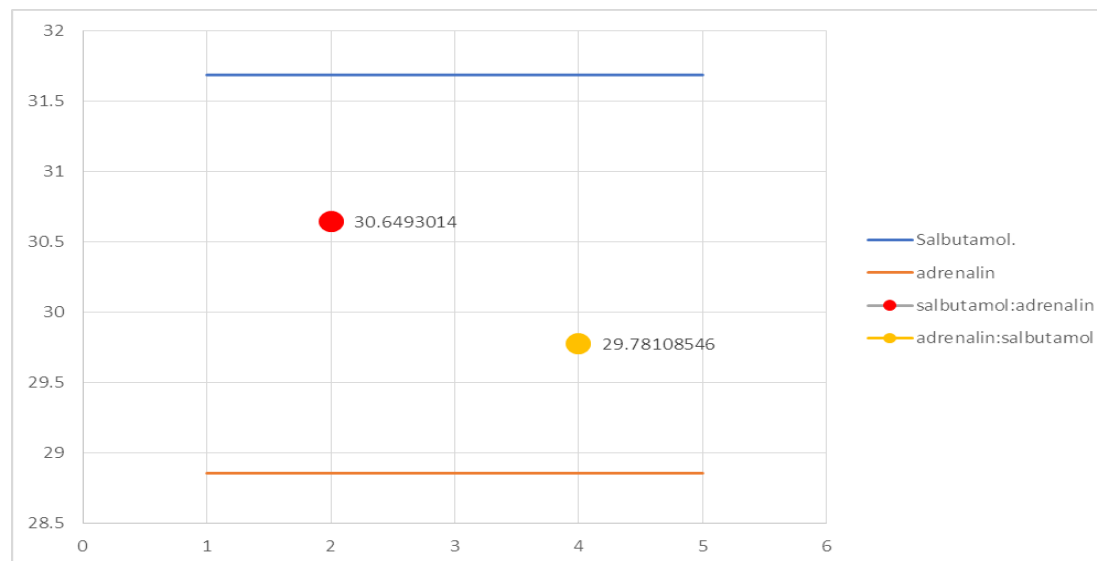


Figure: 1. Shows how SB has an average probability of interacting with adrenaline. We mark the limits (ETC) with the lines blue (SB) and orange (adrenaline).

Table: 4. Due to its ETC = 27.11, SB is observed to act as serotonin oxidant this indicates the highest probability that these substances will interact. The highest recorded ETC is acetylcholine: SB

Table: 4. NT: SB Cross Bands

Reducing Agent	Oxidizing Agent	Homo	Lumo	BG	E-	E+	EP	ETC
ADRENALIN	SALBUTAMOL	-8.998369	0.05508098	9.05344998	-0.117	0.187	0.304	29.78108546
SEROTONIN	SALBUTAMOL	-8.948424	0.05508098	9.00350498	-0.145	0.187	0.332	27.1189909
DOPAMINE	SALBUTAMOL	-8.867786	0.05508098	8.92286698	-0.098	0.187	0.285	31.30830519
GABA	SALBUTAMOL	-9.561541	0.05508098	9.61662198	-0.14	0.187	0.327	29.40862991
GLYCINE	SALBUTAMOL	-9.853025	0.05508098	9.90810598	-0.126	0.187	0.313	31.65529067
ASPARTY ACID	SALBUTAMOL	-10.24183	0.05508098	10.29691098	-0.109	0.187	0.296	34.78686142
GLUTAMIC ACID	SALBUTAMOL	-10.04443	0.05508098	10.09951098	-0.084	0.187	0.271	37.26756819
NORADRENALINE	SALBUTAMOL	-9.151818	0.05508098	9.20689898	-0.083	0.187	0.27	34.09962585
ACETYLCHOLINE	SALBUTAMOL	-9.241984	0.05508098	9.29706498	-0.028	0.187	0.215	43.2421627

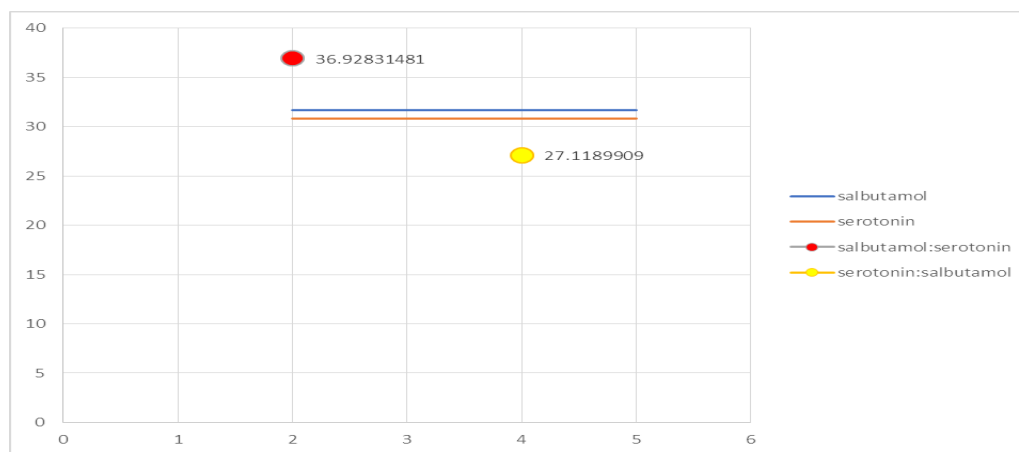


Figure: 2. We determine the red dot as the SB: serotonin ratio this relationship is in a bass probability zone and the yellow dot represents the serotonin: SB interaction which is in an area of high probability. We can see that the blue (SB) and orange (serotonin) lines are very close, which means that SB and serotonin ETC are very similar.

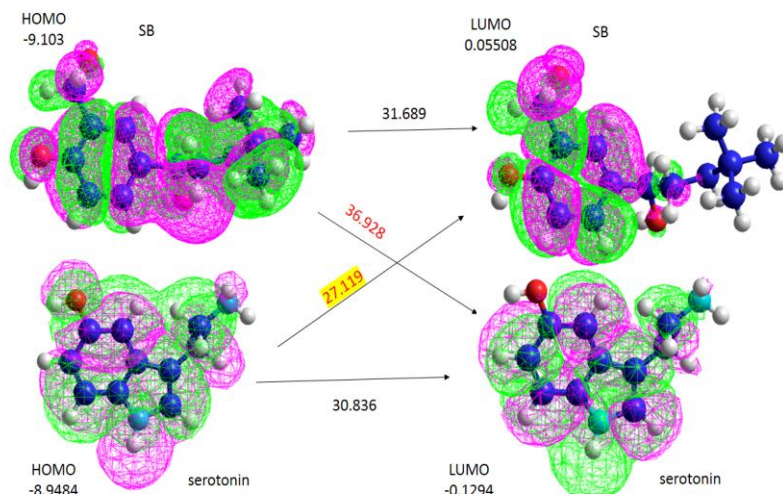


Figure: 3. Exchange of electrons between the SB and serotonin molecules in cross bands.

CONCLUSION

1. According to Table 4, we found that SB acts as an oxidizing agent for serotonin, adrenaline, and GABA because of its low ETCs.
2. The interaction of serotonin: SB was the highest affinity followed by adrenaline and GABA.
3. The serotonin: SB ratio has an ETC of 27,119, the lowest of the two tables because of that it is in a very high probability zone.
4. We observed in Table 3 that the lowest recorded ETC is 30.64 corresponding to SB: adrenaline and is in a medium probability zone.
5. It is highly unlikely that SB will interact as an antioxidant of noradrenaline because it is the highest calculated ETC (Table 3).
6. In Figure 3 we note that the SB molecule has an ETC of 31.68 and the serotonin molecule has an ETC of 30.83.
7. The interaction of SB to serotonin has an ETC of 36,928 while the interaction of serotonin to SB has an ETC of 27,119. Therefore, it is more likely that the serotonin electrons pass through SB.

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