

## References

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## Comparative study between bupivacaine (S75-R25) and ropivacaine to evaluate cardiovascular safety in brachial plexus block: Hamaji A et al.: *Rev Bras Anesthesiol*, 2013;63(4):322–326

Dear Editor,

It was really gratifying for me – I, who am the true author of the ultimate local anesthetic agent obtained worldwide, the enantiomeric mixture of bupivacaine (EMB) or simocain or also novabupi – the efficacy, without the corresponding cardiotoxicity of this product, thanks to the research of my colleagues at the Department of Anesthesia, Hospital de Clinicas, USP (where I come from).

The method used in the research is based on the measurement of important variables for the plexus block technique, which ensures the great relevance of such a research. Therefore, it is a well-conducted clinical work, able to endorse my findings in the preclinical phase of the study of this compound on the aspects of efficacy/safety.

However, some inconsistencies emerge in the writing of this article, such as:

- (a) The authors, when referring to the local anesthetic compared to ropivacaine, committed a historical untruth.

The invention that resulted in the non-equimolar racemic compound formed by antagonistic isomers – the bupivacain enantiomers (S75%:R25%) WAS NOT “created by a Brazilian pharmaceutical company” at all.

In truth, the insight happened in the stands of my lab at the Department of Pharmacology, Institute of Biomedical Sciences, University of São Paulo, and it was also there that I made the application for patenting. As a support for this historical truth, this product was endorsed by INPI (Instituto Nacional de Propriedade Industrial) – the regulatory agency of the Brazilian government – which granted it a patent

and recently confirmed it by charter (Fig. 1).

In the course of writing the article, however, there is a reference to this compound, attributing its origin to the “Brazilian pharmacology, that introduced an enantiomeric mixture of optical isomers containing 75% levobupivacaine (S-) and 25% dextrobupivacaine (R+) – the S75-R25 bupivacaine”.

My question is: What is the group of pharmacologists responsible for this feat? This was not mentioned.

And why the true authorship was omitted, even at the cost of blurring the University of Sao Paulo? The question remains hanging in the air.

Would not be more correct to search the literature, so as not to incur in an enormous blunder which impairs the excellence of the research and thus shakes somehow the reputation of the authors (some of them renowned Professors)? In a quick search of the literature, it would be possible to find reliable studies (among others) and relevant and trustworthy papers, such as:

1. Simonetti MPB, Ferreira FMC. Do the D-isomers of bupivacaine contribute to the improvement of efficacy in neural block? *Reg Anesth Paim Med.* 1999;24(suppl.):43.
2. Simonetti MPB et al. Is it worth manipulating the enantiomeric ratio of bupivacaine to improve the efficacy of the neural block with reduced cardiotoxicity? *Inter Monitor-ESRA.* 1999;11(suppl.): 198.
3. Simonetti MPB. Anestésicos locais espinhais levógiros. In *anestesia peridural, atualização e perspectivas: Delfino J, Vale Nilton. Anestesia peridural: atualização e perspectivas. São Paulo: Editora Atheneu. 2000:81–97.*
4. Simonetti MPB. A epopeia do desenvolvimento dos anestésicos locais em curso de educação a distância em anesthesiologia. Editores: Carraretto A, Viana P. 2007, vol. VII, p. 162–178.
5. Simonetti MPB. Patente: curiosidades vernáculas e história da ideia que foi patenteada e da patente

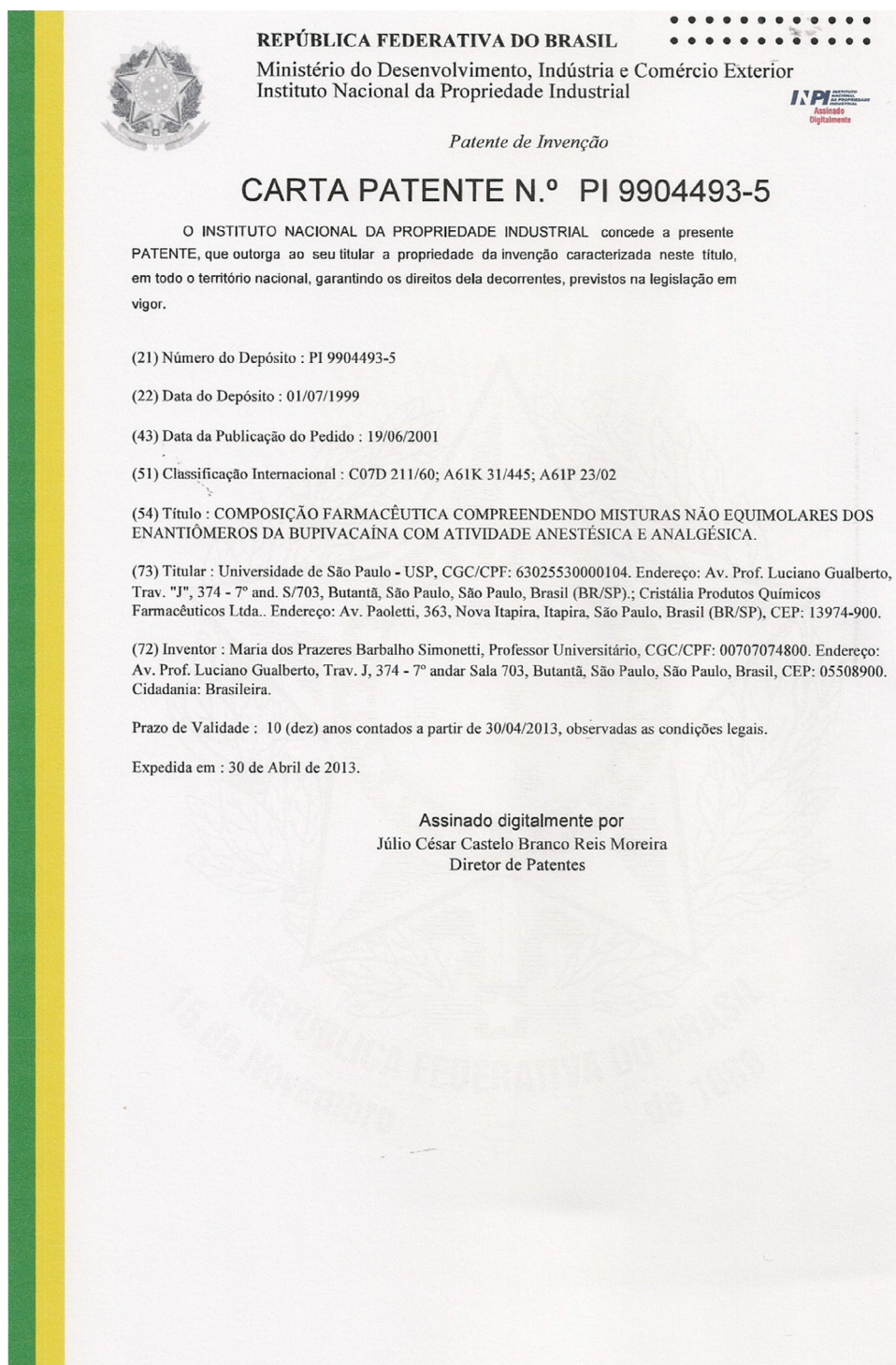


Figure 1 Charter.

que não foi concedida. *Anestesia em Revista*, 2013;2:9–21.

- (b) Meanwhile, the chemical name with which my anesthetic was baptized by the company that sells it has caused embarrassing situations. I called him *Simocain* (S from *left* and *caine*, a suffix used by Neumamm for the crystals of *Erytroxilon coca* leaves and adopted for all local anesthetics obtained since 1855), according

to current nomenclature. However, all that happened was beyond my control, because my invention has been transferred by USP to the Company selling it; and the compound received an inappropriate name, difficult to be cited in scientific articles by being too long, since it encompasses all pharmacotechnique: *levobupivacaine hydrochloride in enantiomeric excess 5%, 75 to 25%...* Whew! Hence the simplification that

Brazilian researchers are now using – calling levobupivacaine (which is another local anesthetic, homochiral, Chirocaine) to the non-equimolar racemic product of bupivacain – the Brazilian local anesthetic. I insist that the agent levobupivacaine obtained by Chirosciences by means of resolution of the equimolar racemate NEVER existed commercially in Brazil.

- (c) Consequences: this semantic error causes confusion to the “referees”, mainly foreign ones, since there are significant differences, for instance, pharmacodynamic and pharmacokinetic ones, between simocain (which is racemic) and levobupivacaine (which is homochiral); moreover, there are also stereoselective differences. There is another aggravating circumstance: the Brazilian anesthetic – Simocain – cannot be compared with results of researches in which homochiral levobupivacaine was effectively used, by the way of conclusion. It would be like comparing completely different entities, or apples with pears... More importantly, of course this inadequacy about the nomenclature can adversely affect the Brazilian research, if there was a pretense of submitting papers to journals abroad (if the error is detected!!!). On the other hand, this is a bad example to our young fellow researchers, who would have to live together with false data... And if that was not enough, this error affects the authors’ reputation of excellence and “bypass” the merits of USP. And further, the error discredits the RBA and its Editorial Board (by allowing that such impropriety is published), because our journal, being bilingual, has broadened its horizons beyond Brazilian borders. We must consider the interest of Turkish authors, who have embarked on this sophistry, drawing on quotations from Brazilian studies in which the nomenclature of the anesthetic is incorrect. Along the same lines and for the reasons already explained, pure levobupivacaine should not be the basis for the

results of S75-R25 as usually the case with many papers, including the article in question.

I hope that the USPian authors recognize the error of this omission to the University of Sao Paulo - which was the birthplace for the first and only patent granted to Brazilian regional anesthesia!

Now I want to invoke the great physiologist Ramon Y Cajal, Nobel Prize 1906, with a transcript of his message – a true libel in defence of intellectual property and surely of great value for the reflection of master trainers of anaesthesiologists and medical researchers:

*“By being a victim of annoying omissions and of unjust silences, we realize that every idea is a scientific creature, whose author, who gave it his life to the cost of great fatigue, cries when seeing his paternity disavowed, with the same cry of that mother who saw snatched from her arms the fruit of her womb.”<sup>1</sup>*

I hope I have contributed without intending anything other than the truth, because as a professional I am well known and, in addition, well-paid with due royalties.

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