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## Pharmacological and clinical implications of FSH isoforms

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The pituitary gland secretes a heterogeneous mixture of FSH isoforms whose properties are affected by glycosylation pattern complexity and the number of sialic acid residues.

The glycosylation pattern of FSH molecules varies in different physiological conditions (e.g. in reproductively competent women and after the menopause) and even within the normal menstrual cycle. Similarly, the glycosylation features of FSH contained in pharmaceutical preparations can be significantly different, thus affecting FSH pharmacokinetics and the overall clinical actions of these drugs.

In general, more acidic isoforms (i.e. containing greater amounts of sialic acid) are secreted in greater amounts after the menopause and during the luteal- follicular transition (at the time of follicle recruitment), while less acidic FSH prevails at the periovulatory stage of the spontaneous menstrual cycle. More acidic isoforms are also contained in human-derived FSH preparations (as they are extracted from the urine of post-menopausal women) while recombinant FSH isoforms are markedly less acidic.

Greater sialic acid content delays FSH catabolism and thus prolongs FSH half-life and activity in blood. Conversely, less-acidic FSH isoforms tend to stimulate steroidogenesis (including progesterone secretion during the follicular phase) more intensely. Although these concepts generally apply to all commercially available FSH preparations (including hMG), novel data seem to indicate that some human-derived highly purified FSH preparations possess unique glycosylation patterns that may positively affect their clinical efficacy.

Thus, it appears that better understanding of FSH structural characteristics and improved purification procedures may help in designing optimally effective medications for the management of reproductive disorders and for the improvement of controlled ovarian stimulation in assisted reproduction procedures.