

Peer Review File

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This is a systematic review which include clinical, nonclinical and in vitro study. Authors selected paper by systematic methods. However, the summarized data obtained from selected papers are not enough for discussion. Following are my minor comments.

Comment 1: Clinical study: Please add study design in table 1 or 2 which indicate the evidence level.

Reply 1: All clinical studies were cohort study designs, level of evidence III. This has been added to Table 1.

Comment 2: Non-clinical study: Please add strain, dosage and body weight in Table 3 or 4 which will affect the outcome.

Reply 2: Strain, dosage, and body weight were added in Table 3 for these nonclinical studies.

Comment 3: In vitro: Please add the concentration of drugs in Table 5 or 6 which will affect the outcome

Reply 3: The concentration of drugs has been added to Table 5 as requested.

Comment 4: Cox-selectivity: Please add the definition of cox-1 selective, cox-2 selective, non-selective. Piroxicam is categorized as cyclooxygenase-1-2 inhibitor in ref 12, but not in this review.

Reply 4: We have operationally defined COX-selectivity in both the Methods and the footnote of Table 2. Details have been placed below for your reference:

Lines 417 to 419: “Selective inhibitors have preferential blockade of either the respective COX-1 (referred to as 1) or COX-2 (referred to as 2) enzyme. Nonselective inhibitors act on both COX enzymes to a significant degree without preferential blockade of either enzyme (referred to as non-selective).”

Comment 5: Secondary outcome should be included in table, because those could provide more detail information.

Reply 5: Secondary outcome measures were added to Table 2.

Comment 6: If available, please update your reference list by including related literatures published within a year. Some of the references are outdated.

Reply 6: All references are up to date per the stated PRISMA guidelines.